```
=> fil reg
FILE 'REGISTRY' ENTERED AT 07:49:27 ON 24 JUN 2002
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
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STRUCTURE FILE UPDATES:   22 JUN 2002  HIGHEST RN 433282-38-3
DICTIONARY FILE UPDATES:  22 JUN 2002  HIGHEST RN 433282-38-3

TSCA INFORMATION NOW CURRENT THROUGH January 7, 2002

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Calculated physical property data is now available.  See HELP PROPERTIES
for more information.  See STNote 27, Searching Properties in the CAS
Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

=> d l86 ide can tot

L86  ANSWER 1 OF 29  REGISTRY  COPYRIGHT 2002 ACS
RN   201211-07-6  REGISTRY
CN   9H-Purine-9-ethanol, 6-amino-.alpha.-methyl-.beta.-(5-phenylpentyl)-,
     (.alpha.S,.beta.R)- (9CI)  (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN   9H-Purine-9-ethanol, 6-amino-.alpha.-methyl-.beta.-(5-phenylpentyl)-,
     [S-(R*,S*)]-
FS   STEREOSEARCH
MF   C19 H25 N5 O
SR   CA
LC   STN Files:   CA, CAPLUS, CASREACT, USPATFULL

Absolute stereochemistry.  Rotation (+).
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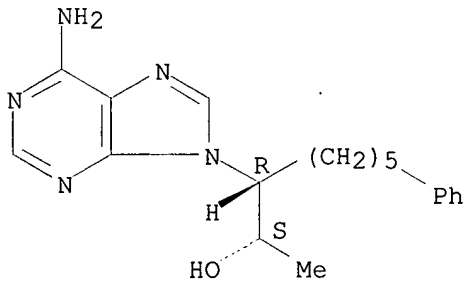


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**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

               3 REFERENCES IN FILE CA (1967 TO DATE)
               3 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE   1:  134:86485

REFERENCE   2:  129:245403

REFERENCE   3:  128:101959

L86  ANSWER 2 OF 29  REGISTRY  COPYRIGHT 2002 ACS
RN   201211-05-4  REGISTRY
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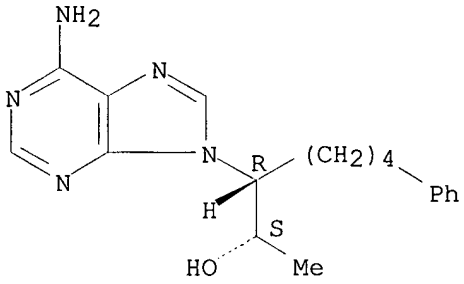
Jan Delaval
Reference Librarian
Biotechnology & Chemical Library
CM1 1E07 – 703-308-4498
jan.delaval@uspto.gov

CN 9H-Purine-9-ethanol, 6-amino-.alpha.-methyl-.beta.-(4-phenylbutyl)-, (.alpha.S,.beta.R)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 9H-Purine-9-ethanol, 6-amino-.alpha.-methyl-.beta.-(4-phenylbutyl)-, [S-(R*,S*)]-
FS STEREOSEARCH
MF C18 H23 N5 O
SR CA
LC STN Files: CA, CAPLUS, CASREACT, USPATFULL

Absolute stereochemistry. Rotation (+).



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

3 REFERENCES IN FILE CA (1967 TO DATE)
3 REFERENCES IN FILE CAPLUS (1967 TO DATE)

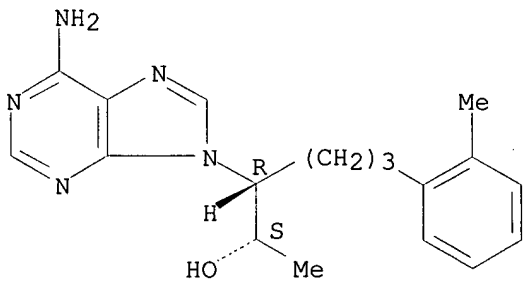
REFERENCE 1: 134:86485

REFERENCE 2: 129:245403

REFERENCE 3: 128:101959

L86 ANSWER 3 OF 29 REGISTRY COPYRIGHT 2002 ACS
RN 201211-04-3 REGISTRY
CN 9H-Purine-9-ethanol, 6-amino-.alpha.-methyl-.beta.-[3-(2-methylphenyl)propyl]-, (.alpha.S,.beta.R)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 9H-Purine-9-ethanol, 6-amino-.alpha.-methyl-.beta.-[3-(2-methylphenyl)propyl]-, [S-(R*,S*)]-
FS STEREOSEARCH
MF C18 H23 N5 O
SR CA
LC STN Files: CA, CAPLUS, CASREACT, USPATFULL

Absolute stereochemistry. Rotation (+).



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

3 REFERENCES IN FILE CA (1967 TO DATE)
3 REFERENCES IN FILE CAPLUS (1967 TO DATE)

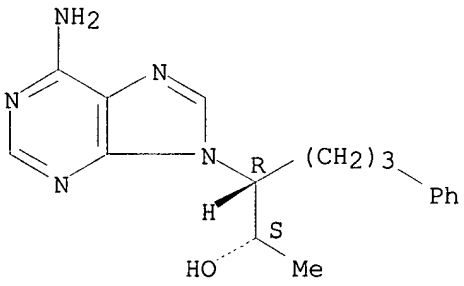
REFERENCE 1: 134:86485

REFERENCE 2: 129:245403

REFERENCE 3: 128:101959

L86 ANSWER 4 OF 29 REGISTRY COPYRIGHT 2002 ACS
RN 201211-02-1 REGISTRY
CN 9H-Purine-9-ethanol, 6-amino-.alpha.-methyl-.beta.-(3-phenylpropyl)-, (.alpha.S,.beta.R)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 9H-Purine-9-ethanol, 6-amino-.alpha.-methyl-.beta.-(3-phenylpropyl)-, [S-(R*,S*)]-
FS STEREOSEARCH
MF C17 H21 N5 O
SR CA
LC STN Files: CA, CAPLUS, CASREACT, USPATFULL

Absolute stereochemistry. Rotation (+).



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

3 REFERENCES IN FILE CA (1967 TO DATE)
3 REFERENCES IN FILE CAPLUS (1967 TO DATE)

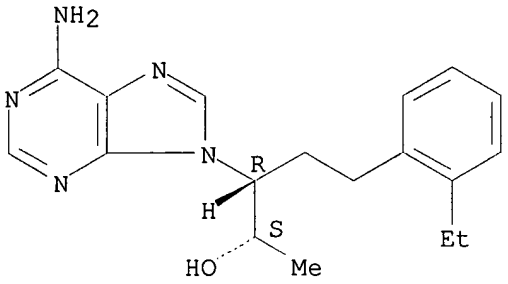
REFERENCE 1: 134:86485

REFERENCE 2: 129:245403

REFERENCE 3: 128:101959

L86 ANSWER 5 OF 29 REGISTRY COPYRIGHT 2002 ACS
RN 201211-00-9 REGISTRY
CN 9H-Purine-9-ethanol, 6-amino-.beta.-[2-(2-ethylphenyl)ethyl]-.alpha.-methyl- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C18 H23 N5 O
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.



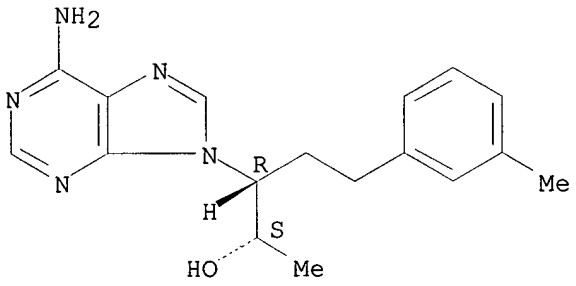
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 128:101959

L86 ANSWER 6 OF 29 REGISTRY COPYRIGHT 2002 ACS
RN 201210-99-3 REGISTRY
CN 9H-Purine-9-ethanol, 6-amino-.alpha.-methyl-.beta.-[2-(3-methylphenyl)ethyl]-, (.alpha.S,.beta.R)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 9H-Purine-9-ethanol, 6-amino-.alpha.-methyl-.beta.-[2-(3-methylphenyl)ethyl]-, [S-(R*,S*)]-
FS STEREOSEARCH
MF C17 H21 N5 O
SR CA
LC STN Files: CA, CAPLUS, CASREACT, USPATFULL

Absolute stereochemistry. Rotation (+).



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

3 REFERENCES IN FILE CA (1967 TO DATE)
3 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:86485

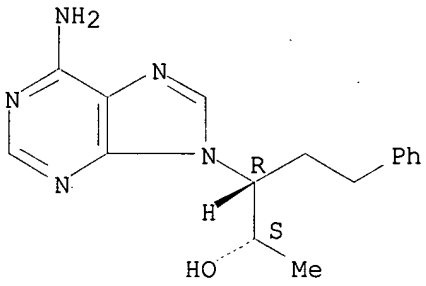
REFERENCE 2: 129:245403

REFERENCE 3: 128:101959

L86 ANSWER 7 OF 29 REGISTRY COPYRIGHT 2002 ACS
RN 201210-97-1 REGISTRY
CN 9H-Purine-9-ethanol, 6-amino-.alpha.-methyl-.beta.-(2-phenylethyl)-, [S-(R*,S*)]- (9CI) (CA INDEX NAME)

FS STEREOSEARCH
MF C16 H19 N5 O
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.



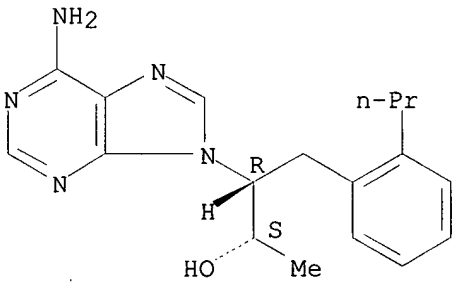
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 128:101959

L86 ANSWER 8 OF 29 REGISTRY COPYRIGHT 2002 ACS
RN 201210-95-9 REGISTRY
CN 9H-Purine-9-ethanol, 6-amino-.alpha.-methyl-.beta.-[(2-propylphenyl)methyl]-, (.alpha.S,.beta.R)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 9H-Purine-9-ethanol, 6-amino-.alpha.-methyl-.beta.-[(2-propylphenyl)methyl]-, [S-(R*,S*)]-
FS STEREOSEARCH
MF C18 H23 N5 O
SR CA
LC STN Files: CA, CAPLUS, CASREACT, USPATFULL

Absolute stereochemistry. Rotation (+).



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

3 REFERENCES IN FILE CA (1967 TO DATE)
3 REFERENCES IN FILE CAPLUS (1967 TO DATE)

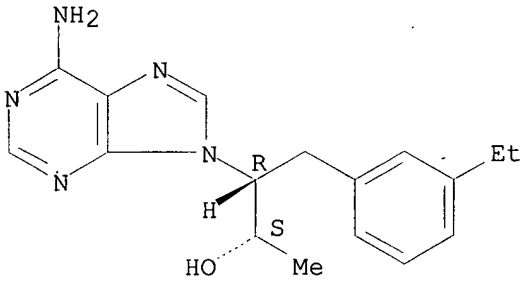
REFERENCE 1: 134:86485

REFERENCE 2: 129:245403

REFERENCE 3: 128:101959

L86 ANSWER 9 OF 29 REGISTRY COPYRIGHT 2002 ACS
RN 201210-93-7 REGISTRY
CN 9H-Purine-9-ethanol, 6-amino-.beta.-[(3-ethylphenyl)methyl]-.alpha.-methyl-, (.alpha.S,.beta.R)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 9H-Purine-9-ethanol, 6-amino-.beta.-[(3-ethylphenyl)methyl]-.alpha.-methyl-, [S-(R*,S*)]-
FS STEREOSEARCH
MF C17 H21 N5 O
SR CA
LC STN Files: CA, CAPLUS, CASREACT, USPATFULL

Absolute stereochemistry. Rotation (+).



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

3 REFERENCES IN FILE CA (1967 TO DATE)
3 REFERENCES IN FILE CAPLUS (1967 TO DATE)

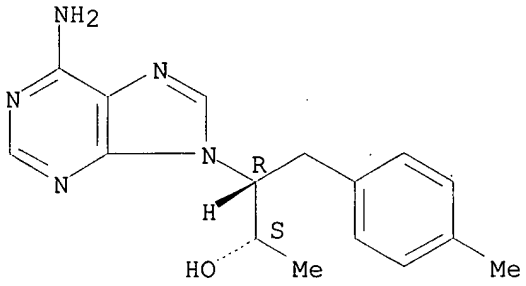
REFERENCE 1: 134:86485

REFERENCE 2: 129:245403

REFERENCE 3: 128:101959

L86 ANSWER 10 OF 29 REGISTRY COPYRIGHT 2002 ACS
RN 201210-91-5 REGISTRY
CN 9H-Purine-9-ethanol, 6-amino-.alpha.-methyl-.beta.-[(4-methylphenyl)methyl]-, (.alpha.S,.beta.R)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 9H-Purine-9-ethanol, 6-amino-.alpha.-methyl-.beta.-[(4-methylphenyl)methyl]-, (R)-
FS STEREOSEARCH
MF C16 H19 N5 O
SR CA
LC STN Files: CA, CAPLUS, CASREACT, USPATFULL

Absolute stereochemistry. Rotation (+).



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

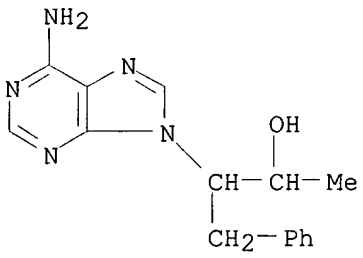
3 REFERENCES IN FILE CA (1967 TO DATE)
3 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:86485

REFERENCE 2: 129:245403

REFERENCE 3: 128:101959

L86 ANSWER 11 OF 29 REGISTRY COPYRIGHT 2002 ACS
RN 200129-88-0 REGISTRY
CN 9H-Purine-9-ethanol, 6-amino-.alpha.-methyl-.beta.-(phenylmethyl)- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C15 H17 N5 O
SR CA
LC STN Files: CA, CAPLUS



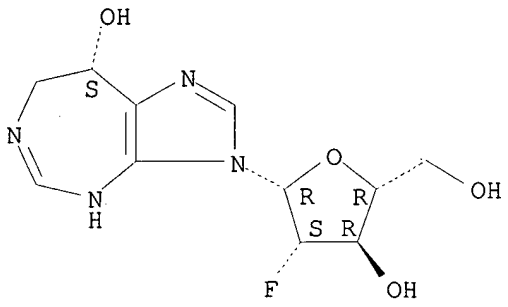
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 128:43435

L86 ANSWER 12 OF 29 REGISTRY COPYRIGHT 2002 ACS
RN 149623-89-2 REGISTRY
CN Imidazo[4,5-d][1,3]diazepin-8-ol, 3-(2-deoxy-2-fluoro-.beta.-D-arabinofuranosyl)-3,4,7,8-tetrahydro-, (S)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF **C11 H15 F N4 O4**
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

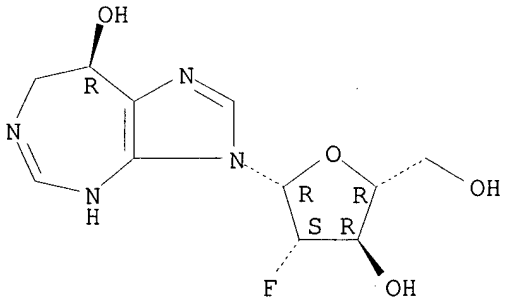
2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 127:248367

REFERENCE 2: 119:139705

L86 ANSWER 13 OF 29 REGISTRY COPYRIGHT 2002 ACS
RN 149623-88-1 REGISTRY
CN Imidazo[4,5-d][1,3]diazepin-8-ol, 3-(2-deoxy-2-fluoro-.beta.-D-arabinofuranosyl)-3,4,7,8-tetrahydro-, (R)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF **C11 H15 F N4 O4**
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

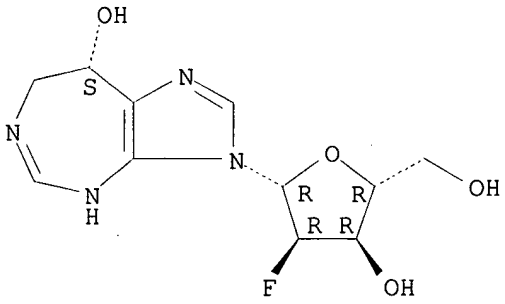
REFERENCE 1: 127:248367

REFERENCE 2: 119:139705

L86 ANSWER 14 OF 29 REGISTRY COPYRIGHT 2002 ACS
RN 149623-87-0 REGISTRY
CN Imidazo[4,5-d][1,3]diazepin-8-ol, 3-(2-deoxy-2-fluoro-.beta.-D-ribofuranosyl)-3,4,7,8-tetrahydro-, (S)- (9CI) (CA INDEX NAME)

FS STEREOSEARCH
MF **C11 H15 F N4 O4**
SR CA
LC STN Files: CA, CAPLUS, CASREACT, TOXCENTER, USPATFULL

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

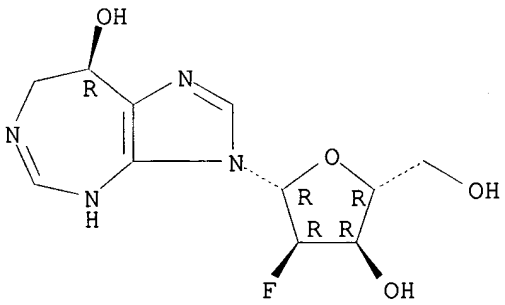
2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 127:248367

REFERENCE 2: 119:139705

L86 ANSWER 15 OF 29 REGISTRY COPYRIGHT 2002 ACS
RN 149623-86-9 REGISTRY
CN Imidazo[4,5-d][1,3]diazepin-8-ol, 3-(2-deoxy-2-fluoro-.beta.-D-ribofuranosyl)-3,4,7,8-tetrahydro-, (R)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF **C11 H15 F N4 O4**
SR CA
LC STN Files: CA, CAPLUS, CASREACT, TOXCENTER, USPATFULL

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

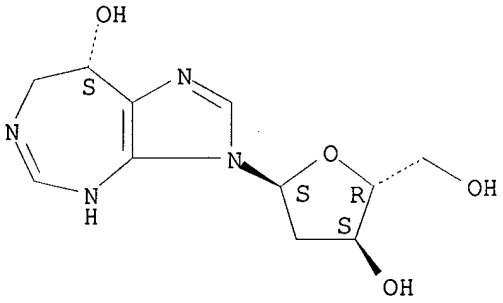
2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 127:248367

REFERENCE 2: 119:139705

L86 ANSWER 16 OF 29 REGISTRY COPYRIGHT 2002 ACS
RN 82264-18-4 REGISTRY
CN Imidazo[4,5-d][1,3]diazepin-8-ol, 3-(2-deoxy-.alpha.-D-erythro-pentofuranosyl)-3,4,7,8-tetrahydro-, (S)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF **C11 H16 N4 O4**
LC STN Files: BEILSTEIN*, CA, CAPLUS
(*File contains numerically searchable property data)

Absolute stereochemistry.



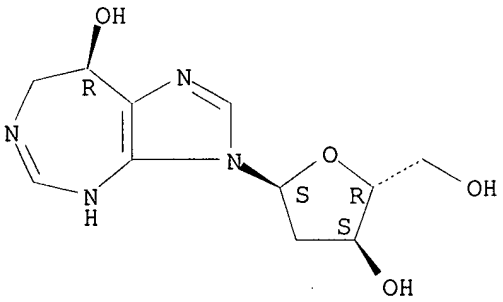
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 97:92686

L86 ANSWER 17 OF 29 REGISTRY COPYRIGHT 2002 ACS
RN 82264-17-3 REGISTRY
CN Imidazo[4,5-d][1,3]diazepin-8-ol, 3-(2-deoxy-.alpha.-D-erythro-pentofuranosyl)-3,4,7,8-tetrahydro-, (R)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF **C11 H16 N4 O4**
LC STN Files: BEILSTEIN*, CA, CAPLUS
(*File contains numerically searchable property data)

Absolute stereochemistry.



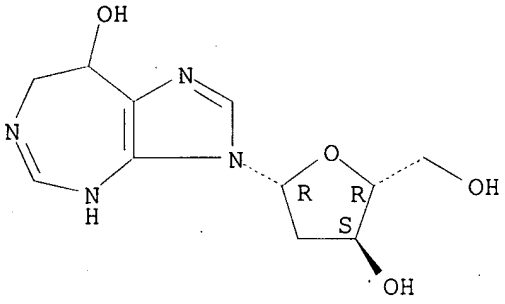
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 97:92686

L86 ANSWER 18 OF 29 REGISTRY COPYRIGHT 2002 ACS
RN 80374-25-0 REGISTRY
CN Imidazo[4,5-d][1,3]diazepin-8-ol, 3-(2-deoxy-.beta.-D-erythro-pentofuranosyl)-3,4,7,8-tetrahydro- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF **C11 H16 N4 O4**
LC STN Files: BEILSTEIN*, CA, CAPLUS
(*File contains numerically searchable property data)

Absolute stereochemistry.



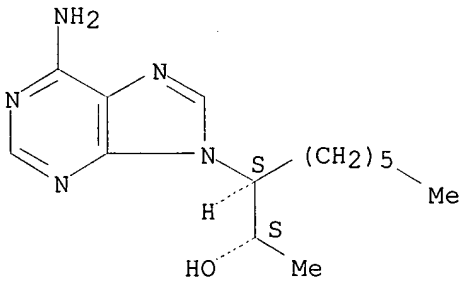
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 96:35675

L86 ANSWER 19 OF 29 REGISTRY COPYRIGHT 2002 ACS
RN 79854-84-5 REGISTRY
CN 9H-Purine-9-ethanol, 6-amino-.beta.-hexyl-.alpha.-methyl-, [S-(R*,R*)]-(9CI) (CA INDEX NAME)
OTHER NAMES:
CN (-)-3-Threo-9-(2-Hydroxy-3-nonyl)adenine
FS STEREOSEARCH
MF **C14 H23 N5 O**
CI COM
LC STN Files: BEILSTEIN*, CA, CAPLUS
(*File contains numerically searchable property data)

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

5 REFERENCES IN FILE CA (1967 TO DATE)
5 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 126:47469

REFERENCE 2: 100:61421

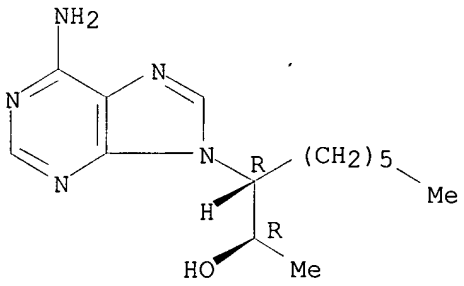
REFERENCE 3: 98:46580

REFERENCE 4: 97:49409

REFERENCE 5: 96:294

L86 ANSWER 20 OF 29 REGISTRY COPYRIGHT 2002 ACS
RN 79854-83-4 REGISTRY
CN 9H-Purine-9-ethanol, 6-amino-.beta.-hexyl-.alpha.-methyl-, [R-(R*,R*)]-
(9CI) (CA INDEX NAME)
OTHER NAMES:
CN (+)-Threo-9-(2-Hydroxy-3-nonyl)adenine
FS STEREOSEARCH
MF **C14 H23 N5 O**
CI COM
LC STN Files: BEILSTEIN*, CA, CAPLUS
(*File contains numerically searchable property data)

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

4 REFERENCES IN FILE CA (1967 TO DATE)
4 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 100:61421

REFERENCE 2: 98:46580

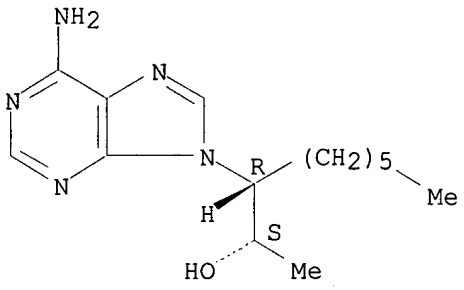
REFERENCE 3: 97:49409

REFERENCE 4: 96:294

L86 ANSWER 21 OF 29 REGISTRY COPYRIGHT 2002 ACS
RN 79813-69-7 REGISTRY
CN 9H-Purine-9-ethanol, 6-amino-.beta.-hexyl-.alpha.-methyl-,
(.alpha.S,.beta.R)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 9H-Purine-9-ethanol, 6-amino-.beta.-hexyl-.alpha.-methyl-, [S-(R*,S*)]-
FS STEREOSEARCH
DR 130573-52-3
MF **C14 H23 N5 O**
CI COM

LC STN Files: BEILSTEIN*, CA, CAPLUS, TOXCENTER
(*File contains numerically searchable property data)

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

15 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
15 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 136:95545

REFERENCE 2: 129:310849

REFERENCE 3: 128:162702

REFERENCE 4: 122:281445

REFERENCE 5: 122:26525

REFERENCE 6: 121:36092

REFERENCE 7: 117:166455

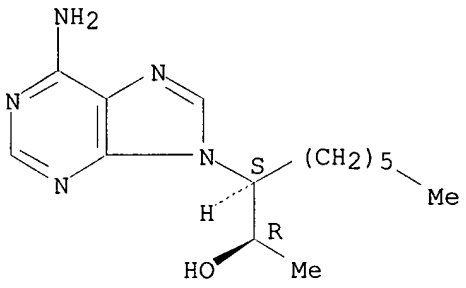
REFERENCE 8: 115:67360

REFERENCE 9: 114:122925

REFERENCE 10: 102:45682

L86 ANSWER 22 OF 29 REGISTRY COPYRIGHT 2002 ACS
RN 79813-68-6 REGISTRY
CN 9H-Purine-9-ethanol, 6-amino-.beta.-hexyl-.alpha.-methyl-, [R-(R*,S*)]-(9CI) (CA INDEX NAME)
OTHER NAMES:
CN (-)-Erythro-9-(2-Hydroxy-3-nonyl)adenine
FS STEREOSEARCH
MF **C14 H23 N5 O**
CI COM
LC STN Files: BEILSTEIN*, BIOSIS, CA, CAPLUS
(*File contains numerically searchable property data)

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

9 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
9 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 117:166455

REFERENCE 2: 114:122925

REFERENCE 3: 106:192259

REFERENCE 4: 105:110667

REFERENCE 5: 100:61421

REFERENCE 6: 98:46580

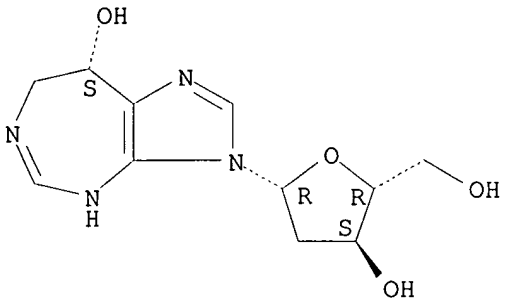
REFERENCE 7: 97:49409

REFERENCE 8: 96:294

REFERENCE 9: 95:199625

L86 ANSWER 23 OF 29 REGISTRY COPYRIGHT 2002 ACS
RN 69196-04-9 REGISTRY
CN Imidazo[4,5-d][1,3]diazepin-8-ol, 3-(2-deoxy-.beta.-D-erythro-pentofuranosyl)-3,4,7,8-tetrahydro-, (8S)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Imidazo[4,5-d][1,3]diazepin-8-ol, 3-(2-deoxy-.beta.-D-erythro-pentofuranosyl)-3,4,7,8-tetrahydro-, (S)-
FS STEREOSEARCH
MF **C11 H16 N4 O4**
LC STN Files: BEILSTEIN*, CA, CAPLUS, IFICDB, IFIPAT, IFIUDB, TOXCENTER
(*File contains numerically searchable property data)

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

7 REFERENCES IN FILE CA (1967 TO DATE)
7 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 131:223047

REFERENCE 2: 114:139620

REFERENCE 3: 113:128535

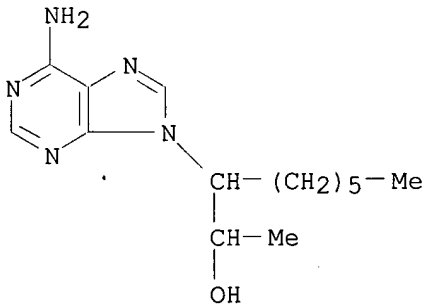
REFERENCE 4: 102:91916

REFERENCE 5: 97:92686

REFERENCE 6: 92:6861

REFERENCE 7: 90:87527

L86 ANSWER 24 OF 29 REGISTRY COPYRIGHT 2002 ACS
RN 59262-86-1 REGISTRY
CN 9H-Purine-9-ethanol, 6-amino-.beta.-hexyl-.alpha.-methyl- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF **C14 H23 N5 O**
CI COM
LC STN Files: BEILSTEIN*, BIOTECHNO, CA, CANCERLIT, CAPLUS, EMBASE, MEDLINE, TOXCENTER, USPATFULL
(*File contains numerically searchable property data)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

4 REFERENCES IN FILE CA (1967 TO DATE)

4 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 128:43435

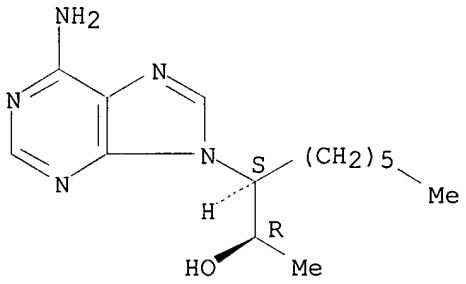
REFERENCE 2: 93:168309

REFERENCE 3: 93:168308

REFERENCE 4: 85:10425

L86 ANSWER 25 OF 29 REGISTRY COPYRIGHT 2002 ACS
RN **55601-18-8** REGISTRY
CN 9H-Purine-9-ethanol, 6-amino-.beta.-hexyl-.alpha.-methyl-, hydrochloride, (.alpha.R,.beta.S)-rel- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 9H-Purine-9-ethanol, 6-amino-.beta.-hexyl-.alpha.-methyl-, hydrochloride, (R*,S*)-
OTHER NAMES:
CN erythro-9-(2-Hydroxy-3-nonyl)adenine hydrochloride
FS STEREOSEARCH
MF C14 H23 N5 O . x Cl H
LC STN Files: BEILSTEIN*, CA, CAPLUS, TOXCENTER, USPATFULL
(*File contains numerically searchable property data)
CRN (51350-19-7)

Relative stereochemistry.



●x HCl

12 REFERENCES IN FILE CA (1967 TO DATE)
12 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 136:241706

REFERENCE 2: 113:224576

REFERENCE 3: 100:207716

REFERENCE 4: 99:16292

REFERENCE 5: 97:108414

REFERENCE 6: 97:1284

REFERENCE 7: 95:215321

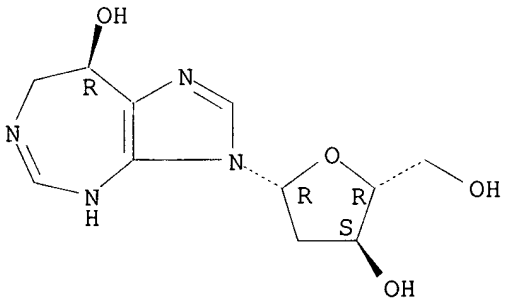
REFERENCE 8: 93:5850

REFERENCE 9: 91:32846

REFERENCE 10: 89:99953

L86 ANSWER 26 OF 29 REGISTRY COPYRIGHT 2002 ACS
RN **53910-25-1** REGISTRY
CN Imidazo[4,5-d][1,3]diazepin-8-ol, 3-(2-deoxy-.beta.-D-erythro-pentofuranosyl)-3,4,7,8-tetrahydro-, (8R)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Imidazo[4,5-d][1,3]diazepin-8-ol, 3-(2-deoxy-.beta.-D-erythro-pentofuranosyl)-3,4,7,8-tetrahydro-, (R)-
OTHER NAMES:
CN 2'-Deoxycoformycin
CN CL 67310465
CN Cl 825
CN Co-Vidarabine
CN Deoxycoformycin
CN Nipent
CN NSC 218321
CN **Pentostatin**
FS STEREOSEARCH
DR 59979-24-7, 63677-95-2, 69196-00-5, 70865-77-9
MF **C11 H16 N4 O4**
CI COM
LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CBNB, CHEMLIST, CIN, DDFU, DIOGENES, DRUGNL, DRUGPAT, DRUGU, DRUGUPDATES, EMBASE, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, NAPRALERT, PHAR, PROMT, RTECS*, TOXCENTER, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: WHO

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

589 REFERENCES IN FILE CA (1967 TO DATE)
18 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
591 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 136:363093

REFERENCE 2: 136:354224

REFERENCE 3: 136:323493

REFERENCE 4: 136:315004

REFERENCE 5: 136:304045

REFERENCE 6: 136:289052

REFERENCE 7: 136:257229

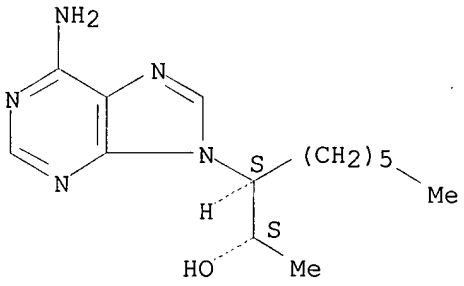
REFERENCE 8: 136:257222

REFERENCE 9: 136:247591

REFERENCE 10: 136:240866

L86 ANSWER 27 OF 29 REGISTRY COPYRIGHT 2002 ACS
RN 51350-21-1 REGISTRY
CN 9H-Purine-9-ethanol, 6-amino-.beta.-hexyl-.alpha.-methyl-, (R*,R*)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF **C14 H23 N5 O**
CI COM
LC STN Files: BEILSTEIN*, CA, CAPLUS
(*File contains numerically searchable property data)

Relative stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

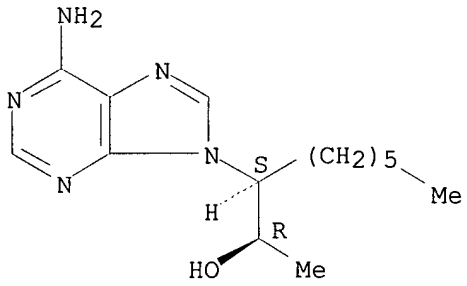
REFERENCE 1: 94:98077

REFERENCE 2: 93:233857

L86 ANSWER 28 OF 29 REGISTRY COPYRIGHT 2002 ACS
RN **51350-19-7** REGISTRY
CN 9H-Purine-9-ethanol, 6-amino-.beta.-hexyl-.alpha.-methyl-, (.alpha.R,.beta.S)-rel- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 9H-Purine-9-ethanol, 6-amino-.beta.-hexyl-.alpha.-methyl-, (R*,S*)-
OTHER NAMES:
CN (.+-.)-Erythro-9-(2-Hydroxy-3-nonyl)adenine
CN 9-erythro-(2-Hydroxyl-3-nonyl)adenine
CN **EHNA**
CN erythro-9-(2-Hydroxy-3-nonyl)adenine
CN erythro-9-(2-Hydroxyl-3-nonyl)adenine
CN NSC 263165
FS STEREOSEARCH
DR 79763-32-9

MF **C14 H23 N5 O**
CI COM
LC STN Files: AGRICOLA, BEILSTEIN*, BIOBUSINESS, BIOSIS, CA, CAPLUS, CEN, CHEMCATS, CSCHEM, DDFU, DRUGU, IPA, MSDS-OHS, TOXCENTER, USPAT2, USPATFULL
(*File contains numerically searchable property data)

Relative stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

230 REFERENCES IN FILE CA (1967 TO DATE)
3 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
230 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 136:380107

REFERENCE 2: 136:350463

REFERENCE 3: 136:322438

REFERENCE 4: 136:247591

REFERENCE 5: 136:241706

REFERENCE 6: 136:128775

REFERENCE 7: 135:339217

REFERENCE 8: 135:286667

REFERENCE 9: 135:41047

REFERENCE 10: 134:262198

L86 ANSWER 29 OF 29 REGISTRY COPYRIGHT 2002 ACS
RN **9026-93-1** REGISTRY
CN Deaminase, adenosine (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Adenosine aminohydrolase
CN Adenosine deaminase
CN Deoxyadenosine deaminase
CN E.C. 3.5.4.4
MF Unspecified
CI MAN
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, DDFU, DRUGU, EMBASE, IFICDB, IFIPAT, IFIUDB, IPA, MSDS-OHS,

PHAR, PROMT, TOXCENTER, USPAT2, USPATFULL
Other Sources: EINECS**
(**Enter CHEMLIST File for up-to-date regulatory information)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
3501 REFERENCES IN FILE CA (1967 TO DATE)
56 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
3508 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 136:399634

REFERENCE 2: 136:397665

REFERENCE 3: 136:396352

REFERENCE 4: 136:364901

REFERENCE 5: 136:364884

REFERENCE 6: 136:364588

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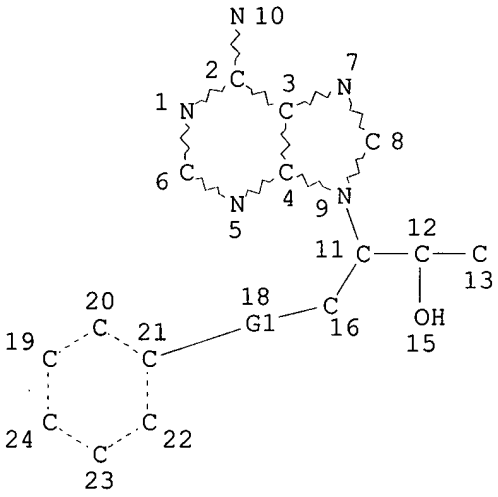
REFERENCE 9: 136:325771

REFERENCE 10: 136:323226

=> d sta que l16
L14 STR



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NODE ATTRIBUTES:
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DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 22

STEREO ATTRIBUTES: NONE
L16 11 SEA FILE=REGISTRY CSS FUL L14

100.0% PROCESSED 531 ITERATIONS 11 ANSWERS
SEARCH TIME: 00.00.01

=> fil hcaplus
FILE 'HCAPLUS' ENTERED AT 07:49:58 ON 24 JUN 2002
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 24 Jun 2002 VOL 136 ISS 26
FILE LAST UPDATED: 21 Jun 2002 (20020621/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

CAS roles have been modified effective December 16, 2001. Please check your SDI profiles to see if they need to be revised. For information on CAS roles, enter HELP ROLES at an arrow prompt or use the CAS Roles thesaurus (/RL field) in this file.

=> d all tot l84

L84 ANSWER 1 OF 13 HCAPLUS COPYRIGHT 2002 ACS
AN **2002:371580** HCAPLUS
TI Inhibiting **adenosine deaminase** modulates the **systemic inflammatory response syndrome** in **endotoxemia** and **sepsis**
AU Adanin, Simon; Yalovetskiy, Igor V.; Nardulli, Beth A.; Sam, Albert D., II; Jonjev, Zivojin S.; **Law, William R.**
CS Departments of Physiology and Biophysics, University of Illinois College of Medicine, Chicago, IL, 60612, USA
SO American Journal of Physiology (2002), 282(5, Pt. 2), R1324-R1332
CODEN: AJPHAP; ISSN: 0002-9513
PB American Physiological Society
DT Journal
LA English
CC 15 (Immunochemistry)
AB By pharmacol. manipulation of endogenous adenosine, using chem. distinct methods, we tested the hypothesis that endogenous adenosine tempers **proinflammatory** cytokine **responses** and oxyradical-mediated tissue damage during **endotoxemia** and **sepsis**. Rats were pretreated with varying doses of **pentostatin** (PNT; **adenosine deaminase** inhibitor) or 8-sulfophenyltheophylline (8-SPT; adenosine receptor

antagonist) and then received either E. coli endotoxin (lipopolysaccharide; 0.01 or 2.0 mg/kg) or a slurry of cecal matter in 5% dextrose in water (200 mg/kg). Resultant levels of tumor necrosis factor (TNF)-.alpha., interleukin (IL)-1.beta., and IL-10 were measured in serum and in liver and spleen. Untreated, 2 mg/kg lipopolysaccharide elevated serum TNF-.alpha., IL-1.beta., and IL-10. PNT dose dependently attenuated, without ablating, the elevation in serum TNF-.alpha. and IL-1.beta. and raised liver and spleen IL-10. PNT also attenuated elevation of TNF-.alpha. in serum, liver, and spleen at 4 and 24 h after **sepsis** induction, and 8-SPT resulted in higher **proinflammatory** cytokines. Modulating endogenous adenosine was also effective in exacerbated (8-SPT) or diminished (PNT) tissue peroxidn. Survival from **sepsis** was also improved when PNT was used as a posttreatment. These data indicate that endogenous adenosine is an important modulatory component of **systemic inflammatory response syndromes**. These data also indicate that inhibition of **adenosine deaminase** may be a novel and viable therapeutic approach to managing the **systemic inflammatory response syndrome** without ablating important physiol. functions.

RE.CNT 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) Arvidsson, S; Acta Chir Scand 1990, V156, P215 MEDLINE
(2) Barankiewicz, J; Eur J Immunol 1985, V15, P627 HCAPLUS
(3) Brackett, L; Biochem Pharmacol 1990, V39, P1897 HCAPLUS
(4) Brogden, R; Drugs 1993, V46, P652 MEDLINE
(5) Broner, C; Circ Shock 1989, V29, P77 HCAPLUS
(6) Castillo, M; Am Surg 1991, V57, P313 MEDLINE
(7) Cronstein, B; Arthritis Rheum 1995, V38, P1040 HCAPLUS
(8) Cronstein, B; J Immunol 1992, V148, P2201 HCAPLUS
(9) Daly, J; J Med Chem 1985, V28, P487 HCAPLUS
(10) Dziki, A; Circ Shock 1993, V39, P29 HCAPLUS
(11) Eigler, A; Scand J Immunol 1997, V45, P132 HCAPLUS
(12) Firestein, G; J Immunol 1994, V152, P5853 HCAPLUS
(13) Hasko, G; J Immunol 1996, V157, P4634 HCAPLUS
(14) Haynes, J; J Pharmacol Exp Ther 1996, V276, P752 HCAPLUS
(15) Itoh, K; Tohoku J Exp Med 1989, V157, P205 HCAPLUS
(16) Law, W; US 6103702 2000 HCAPLUS
(17) Law, W; Cardiovasc Res 1991, V25, P151 HCAPLUS
(18) Law, W; Shock 1997, V3, P217
(19) LeMoine, O; J Immunol 1996, V156, P4408 HCAPLUS
(20) Leff, J; Lancet 1993, V341, P777 MEDLINE
(21) Martin, C; Crit Care Med 2001, V28, P3198
(22) McWhinney, C; Eur J Pharmacol 1996, V310, P209 HCAPLUS
(23) Morgan, R; Circ Shock 1988, V25, P319 HCAPLUS
(24) Motew, S; J Surg Res 1998, V80, P326 HCAPLUS
(25) Motew, S; Shock 1997, V7, P439 MEDLINE
(26) Mourelatos, M; Shock 1996, V5, P141 MEDLINE
(27) Ohkawa, H; Anal Biochem 1979, V95, P351 HCAPLUS
(28) Parmely, M; J Immunol 1993, V151, P389 HCAPLUS
(29) Peralta, J; Circ Shock 1993, V39, P153 HCAPLUS
(30) Read, R; J Antimicrob Chemother 1998, V41, P65 HCAPLUS
(31) Riches, D; J Leukoc Biol 1985, V37, P545 HCAPLUS
(32) Richter, J; J Leukoc Biol 1992, V51, P270 HCAPLUS
(33) Ritchie, P; Cytokine 1997, V9, P187 HCAPLUS
(34) Sajjadi, F; J Immunol 1996, V156, P3435 HCAPLUS
(35) Sam, A; Crit Care Med 2000, V28, P1931
(36) Sam, A; J Surg Res 2000, V94, P61 HCAPLUS
(37) Schiller, H; Crit Care Med 1993, V21, PS92 MEDLINE
(38) Xu, D; J Trauma 1993, V34, P676 HCAPLUS
(39) Zager, R; Circ Res 1991, V68, P185 HCAPLUS

L84 ANSWER 2 OF 13 HCAPLUS COPYRIGHT 2002 ACS

AN 2000:568523 HCAPLUS
DN 133:172177
TI Use of **adenosine deaminase** inhibitors to treat **systemic inflammatory response syndrome**
IN **Law, William R.**
PA Board of Trustees of the University of Illinois, USA
SO U.S., 15 pp.
CODEN: USXXAM
DT Patent
LA English
IC ICM A61K031-70
NCL 514046000
CC 1-7 (Pharmacology)
Section cross-reference(s): 7
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 6103702	A	20000815	US 1999-317678	19990524
WO 2000071127	A1	20001130	WO 2000-US13987	20000522
W: AU, CA, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 1181019	A1	20020227	EP 2000-936154	20000522
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
PRAI US 1999-317678	A1	19990524		
WO 2000-US13987	W	20000522		

AB Methods of treating various-**inflammatory** conditions, including **systemic inflammatory response syndrome (SIRS)**, **septic shock** and burns, conditions which may be ameliorated by increased local concns. of adenosine using **adenosine deaminase** inhibitors are provided. **Pentostatin** inhibited **adenosine deaminase** and attenuated **sepsis** in rats.

ST **adenosine deaminase** inhibitor **systemic inflammatory response syndrome; septic shock** treatment **adenosine deaminase** inhibitor; burn treatment **adenosine deaminase** inhibitor; **pentostatin sepsis** attenuation

IT **Blood**
(**flow** of; use of **adenosine deaminase** inhibitors to treat **systemic inflammatory response syndrome**)

IT Lipids, biological studies
RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(peroxidn. products; use of **adenosine deaminase** inhibitors to treat **systemic inflammatory response syndrome**)

IT Tumor necrosis factors
RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(redn. of levels of; use of **adenosine deaminase** inhibitors to treat **systemic inflammatory response syndrome**)

IT **Shock (circulatory collapse)**
(**septic**; use of **adenosine deaminase** inhibitors to treat **systemic inflammatory response syndrome**)

IT **Inflammation**

(**systemic inflammatory response syndrome**; use of **adenosine deaminase** inhibitors to treat **systemic inflammatory response syndrome**)

IT Anti-**inflammatory** agents
Burn
Mammal (Mammalia)
(use of **adenosine deaminase** inhibitors to treat **systemic inflammatory response syndrome**)

IT Adenosine receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(use of **adenosine deaminase** inhibitors to treat **systemic inflammatory response syndrome**)

IT **9026-93-1, Adenosine deaminase**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibitor of; use of **adenosine deaminase** inhibitors to treat **systemic inflammatory response syndrome**)

IT 504-17-6, Thiobarbituric acid
RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(substances reactive with, redn. of levels of; use of **adenosine deaminase** inhibitors to treat **systemic inflammatory response syndrome**)

IT 80206-91-3
RL: ADV (Adverse effect, including toxicity); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(use of **adenosine deaminase** inhibitors to treat **systemic inflammatory response syndrome**)

IT 58-61-7, Adenosine, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(use of **adenosine deaminase** inhibitors to treat **systemic inflammatory response syndrome**)

IT **51350-19-7, EHNA 53910-25-1, Pentostatin**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(use of **adenosine deaminase** inhibitors to treat **systemic inflammatory response syndrome**)

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Abushanab; US 5703084 1997 HCAPLUS
(2) Anon; WO 9823267 1997 HCAPLUS
(3) Erion; US 5731432 1998 HCAPLUS

L84 ANSWER 3 OF 13 HCAPLUS COPYRIGHT 2002 ACS
AN **2000:445275** HCAPLUS
DN **133:305425**
TI **Adenosine deaminase** inhibition attenuates **reperfusion** low flow and improves graft survival after rat liver transplantation
AU Tian, Ying Hua; Schafer, Thilo; Sckell, Axel; Schilling, Martin K.
CS Departments of Visceral- and Transplantation Surgery and Clinical

Research, University of Bern, Inselspital, Bern, Switz.
SO Transplantation (2000), 69(11), 2277-2281
CODEN: TRPLAU; ISSN: 0041-1337
PB Lippincott Williams & Wilkins
DT Journal
LA English
CC 1-8 (Pharmacology)
AB Background: Low **flow** or no **flow** is a prefinal step after **reperfusion** of hepatic allografts. Adenosine is an intrinsic key regulator of physiol. and pathol. hepatic **blood flow**. Methods: In a model of rat liver transplantation, the effect of donor pretreatment with **adenosine deaminase** inhibitors (0, 0.1, 1, 10 .mu.mol **erythro-9-[2-hydroxy-3-nonyl]adenine**) was studied on hepatic interstitial adenosine concns., **microcirculatory flow**, leukocyte adhesion, and graft survival by means of microdialysis sampling, intravital video microscopy, and laser Doppler **flowmetry**. Results: Donor pretreatment with 1 .mu.mol **erythro-9-[2-hydroxy-3-nonyl]adenine** increased interstitial adenosine concns. 5- to 10-fold, for more than 24 h of cold storage. In LDF studies, mean donor **blood flow** was increased from 420.+-.42 **perfusion** units (PU) to 832.+-.52 PU and from 475.+-.79 to 720.+-.81 PU after **reperfusion**, and in intravital video microscopy studies from 247.+-.24 to 281.+-.39 pl/s. There was no difference in the no. of leukocytes sticking, but a significantly lower percentage of leukocytes rolling (26.1.+-.1.9 vs. 36.5.+-.7.5%) along the endothelial wall in the treatment group. Transplant survival after 44 h cold storage in UW soln. was 8/10 in the treatment group and 1/13 in the control group. Conclusions: Donor pretreatment with **erythro-9-[2-hydroxy-3-nonyl]adenine** increases survival of critically injured liver grafts. Donor or recipient treatment rather than addn. of protectants to cold storage solns. are successful strategies to overcome preservation injury and possibly adverse donor factors.
ST **adenosine deaminase reperfusion** liver graft preservation
IT Anti-ischemic agents
Cryopreservation
Organ preservation
(**adenosine deaminase** inhibition attenuates **reperfusion** low flow and improves liver graft survival)
IT Leukocyte
(adhesion; **adenosine deaminase** inhibition attenuates **reperfusion** low flow and improves liver graft survival)
IT **Reperfusion**
(injury; **adenosine deaminase** inhibition attenuates **reperfusion** low flow and improves liver graft survival)
IT Cell adhesion
(leukocyte; **adenosine deaminase** inhibition attenuates **reperfusion** low flow and improves liver graft survival)
IT Transplant and Transplantation
Transplant and Transplantation
(liver; **adenosine deaminase** inhibition attenuates **reperfusion** low flow and improves liver graft survival)
IT Leukocyte
(rolling; **adenosine deaminase** inhibition attenuates **reperfusion** low flow and improves liver graft survival)
IT Liver
Liver
(transplant; **adenosine deaminase** inhibition

attenuates **reperfusion** low flow and improves liver graft survival)

IT **51350-19-7, erythro-9-[2-Hydroxy-3-nonyl]adenine**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**adenosine deaminase** inhibition attenuates **reperfusion** low flow and improves liver graft survival)

IT 58-61-7, Adenosine, biological studies **9026-93-1, Adenosine deaminase**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**adenosine deaminase** inhibition attenuates **reperfusion** low flow and improves liver graft survival)

RE.CNT 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD

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L84 ANSWER 4 OF 13 HCAPLUS COPYRIGHT 2002 ACS
AN **2000:110911** HCAPLUS
DN **132:146339**
TI Treatment of hairy cell leukemia with cladribine (2-chlorodeoxyadenosine)
AU Fureder, Wolfgang; Weltermann, Ansgar; Chott, Andreas; Gisslinger, Heinz; Valent, Peter; Jager, Ulrich; Geissler, Klaus; Lechner, Klaus
CS Department of Internal Medicine I, Division of Hematology & Hemostaseology, University of Vienna, Austria
SO Wiener Klinische Wochenschrift (1999), 111(24), 1027-1030
CODEN: WKWOAO; ISSN: 0043-5325
PB Springer-Verlag Wien
DT Journal
LA English

CC 1-6 (Pharmacology)
AB Hairy cell leukemia is a rare lymphoproliferative disorder resistant to conventional chemotherapeutic agents. Recently, the purine analog cladribine (2-chlorodeoxyadenosine, 2-CdA) was introduced for the treatment of this disease. We report on 14 patients with hairy cell leukemia who were treated with 2-CdA at our department between 1993 and 1997. The patients received a single cycle of 2-CdA at a dose of 0.07 or 0.09 mg/kg/day by continuous infusion, over a seven-day period. Five patients were previously untreated, while the others had received prior treatment with interferon-.alpha. (seven patients), interferon-.alpha. and splenectomy (one patient) or interferon-.alpha., splenectomy and **pentostatin** (one patient). Six patients achieved complete remission, three a good partial response and three partial remission. Two patients did not respond to treatment and one of them died from **septicemia** in aplasia. Relapse of the disease occurred in two patients. Side effects such as fever (WHO grade 2) and/or neutropenia (WHO grade 4) were noted in eight patients. Thus, 2-CdA is an effective treatment of hairy cell leukemia that can induce long lasting remissions in both, previously treated and untreated patients.
ST cladribine chlorodeoxyadenosine hairy cell leukemia antitumor
IT Leukemia
(hairy-cell, inhibitors; treatment of hairy cell leukemia with cladribine in humans)
IT Antitumor agents
(treatment of hairy cell leukemia with cladribine in humans)
IT 4291-63-8, Cladribine
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(treatment of hairy cell leukemia with cladribine in humans)
RE.CNT 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
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L84 ANSWER 5 OF 13 HCAPLUS COPYRIGHT 2002 ACS

AN **1998:385500** HCAPLUS
DN **129:49654**
TI Use of hydroxyguanidines for treatment or prevention of an ischemic disease
IN Wikberg, Jarl; Prusis, Peteris; Dambrova, Maija; Uhlen, Staffan
PA Wapharm AB, Swed.; Wikberg, Jarl; Prusis, Peteris; Dambrova, Maija; Uhlen, Staffan
SO PCT Int. Appl., 75 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K031-155
ICS A61K031-045; A01N001-02; C07C281-16; C07D249-14; C07D307-52; C07D213-42; C07D207-335
CC 1-8 (Pharmacology)
Section cross-reference(s): 23
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9823267	A1	19980604	WO 1997-SE1969	19971121
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9851430	A1	19980622	AU 1998-51430	19971121
	AU 742969	B2	20020117		
	EP 1007025	A1	20000614	EP 1997-946211	19971121
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, LV, FI				
	JP 2001505209	T2	20010417	JP 1998-524603	19971121
PRAI	SE 1996-4348	A	19961126		
	WO 1997-SE1969	W	19971121		

OS MARPAT 129:49654
AB Hydroxyguanidines are useful for the manuf. of a medicament for treatment or prevention of an ischemic disease condition including an ischemic condition caused by surgery or other therapy and being assocd. with the prodn. of oxygen-derived radicals, the disease condition being a xanthine oxidase/xanthine dehydrogenase-mediated ischemic condition selected from heart infarction, angina pectoris, cerebrovascular infarction, **circulatory shock**, etc. Preferred hydroxyguanidines are carbimino hydroxyguanidines, in particular aryl carbimino hydroxyguanidines. Also disclosed are corresponding methods of treatment, including extracorporeal treatment of organs, and a no. of hydroxyguanidines and their prepn. The presence of 100 .mu.M guanoxabenz resulted in about 60% redn. of superoxide formation by xanthine oxidase in the presence of oxygen.
ST ischemia treatment hydroxyguanidine compd; guanoxabenz superoxide formation inhibition
IT **Heart, disease**
(angina pectoris; hydroxyguanidines for treatment or prevention of ischemic diseases)
IT Brain, disease
(cerebrovascular, ischemic attacks in; hydroxyguanidines for treatment or prevention of ischemic diseases)
IT Radical scavengers
(concomitant drug; hydroxyguanidines for treatment or prevention of ischemic diseases)
IT Lung, disease
(embolism; hydroxyguanidines for treatment or prevention of ischemic

diseases)
IT Spleen
(hydroxyguanidine-reducing activity in; hydroxyguanidines for treatment or prevention of ischemic diseases)
IT Antiarrhythmics
Hypoxia, animal
Ischemia
Shock (circulatory collapse)
Transplant and Transplantation
(hydroxyguanidines for treatment or prevention of ischemic diseases)
IT Brain, disease
Heart, disease
(infarction; hydroxyguanidines for treatment or prevention of ischemic diseases)
IT Surgery
(ischemia from; hydroxyguanidines for treatment or prevention of ischemic diseases)
IT Intestine, disease
(obstruction, bowel torsion with strangulation; hydroxyguanidines for treatment or prevention of ischemic diseases)
IT **Artery, disease**
(**occlusion**; hydroxyguanidines for treatment or prevention of ischemic diseases)
IT Oxidation
(of adenine nucleotide; hydroxyguanidines for treatment or prevention of ischemic diseases)
IT Newborn
(premature; hydroxyguanidines for treatment or prevention of ischemic diseases)
IT **Heart**
(surgery; hydroxyguanidines for treatment or prevention of ischemic diseases)
IT **Embolism**
(thromboembolism; hydroxyguanidines for treatment or prevention of ischemic diseases)
IT Testis, disease
(torsion; hydroxyguanidines for treatment or prevention of ischemic diseases)
IT 50-81-7, Vitamin C, biological studies 67-68-5, DMSO, biological studies 69-93-2, Uric acid, biological studies 70-18-8, Glutathione, biological studies 616-91-1, N-Acetyl-cysteine 1406-18-4, Vitamin E 3376-24-7, N-tert-Butyl-.alpha.-phenylnitrone 9001-05-2, Catalase 9054-89-1, Superoxide dismutase 9054-89-1D, Superoxide dismutase, mimetics **51350-19-7, EHNA 53910-25-1, 2'-Deoxycoformycin** 61805-96-7, Dimethylthiourea
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(concomitant drug; hydroxyguanidines for treatment or prevention of ischemic diseases)
IT 69-89-6, Xanthine
RL: RCT (Reactant); RACT (Reactant or reagent)
(guanoxabenz in xanthine oxidase oxidn. of; hydroxyguanidines for treatment or prevention of ischemic diseases)
IT 11062-77-4, Superoxide
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(guanoxabenz inhibition of formation of; hydroxyguanidines for treatment or prevention of ischemic diseases)
IT 24047-25-4P, Guanoxabenz
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); RACT (Reactant or reagent); USES (Uses)
(hydroxyguanidines for treatment or prevention of ischemic diseases)

IT 13115-21-4, Hydroxyguanidine
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(hydroxyguanidines for treatment or prevention of ischemic diseases)
IT 208583-06-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(hydroxyguanidines for treatment or prevention of ischemic diseases)
IT 87861-78-7P 87861-80-1P 87861-86-7P 87861-88-9P 96826-59-4P
96826-60-7P 102998-00-5P 123541-04-8P 123541-10-6P 139613-33-5P
139613-35-7P 139613-37-9P 139613-39-1P 139613-43-7P 139613-49-3P
139613-51-7P 139613-53-9P 208582-66-5P 208582-67-6P 208582-68-7P
208582-69-8P 208582-70-1P 208582-71-2P 208582-72-3P 208582-73-4P
208582-74-5P 208582-75-6P 208582-76-7P 208582-77-8P 208582-78-9P
208582-79-0P 208582-80-3P 208582-81-4P 208582-82-5P 208582-83-6P
208582-84-7P 208582-85-8P 208582-86-9P 208582-87-0P 208582-88-1P
208582-89-2P 208582-90-5P 208582-91-6P 208582-92-7P 208582-93-8P
208582-94-9P 208582-95-0P 208582-96-1P 208582-97-2P 208582-98-3P
208582-99-4P 208583-00-0P 208583-01-1P 208583-02-2P 208583-03-3P
208583-04-4P 208583-05-5P 208583-07-7P 208583-08-8P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(hydroxyguanidines for treatment or prevention of ischemic diseases)
IT 5051-62-7, Guanabenz
RL: BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative)
(hydroxyguanidines for treatment or prevention of ischemic diseases)
IT 16077-49-9 36826-58-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(hydroxyguanidines for treatment or prevention of ischemic diseases)
IT 13115-21-4D, Hydroxyguanidine, derivs. 208582-65-4D, derivs.
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(hydroxyguanidines for treatment or prevention of ischemic diseases)
IT **9026-93-1, Adenosine deaminase**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibitor, concomitant drug; hydroxyguanidines for treatment or prevention of ischemic diseases)
IT 7782-44-7D, Oxygen, radicals, biological studies
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(ischemia assocd. with; hydroxyguanidines for treatment or prevention of ischemic diseases)
IT 9002-17-9, Xanthine oxidase 9054-84-6, Xanthine dehydrogenase
RL: ADV (Adverse effect, including toxicity); CAT (Catalyst use); BIOL (Biological study); USES (Uses)
(ischemia assocd. with; hydroxyguanidines for treatment or prevention of ischemic diseases)
IT 73-24-5, Adenine, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(oxidn. of, by hydroxyguanidine; hydroxyguanidines for treatment or prevention of ischemic diseases)
IT 315-30-0, Allopurinol 2465-59-0, Oxypurinol 82114-19-0, Amflutizole
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(xanthine oxidase and/or xanthine dehydrogenase blocking drug, concomitant drug; hydroxyguanidines for treatment or prevention of ischemic diseases)

L84 ANSWER 6 OF 13 HCAPLUS COPYRIGHT 2002 ACS
AN 1996:493820 HCAPLUS
DN 125:192332
TI Myocardial stunning and preconditioning during non-cardioplegic warm intermittent aortic cross-clamping

AU Abd-Elfattah, Anwar-Saad A.; Wechsler, Andrew S.
CS Medical College Virginia, Virginia Commonwealth University, Richmond, VA, USA
SO Dev. Cardiovasc. Med. (1996), 181(Purines and Myocardial Protection), 513-523
CODEN: DCMEDM; ISSN: 0166-9842
DT Journal
LA English
CC 14-2 (Mammalian Pathological Biochemistry)
AB In clin. cardiac surgery, warm intermittent aortic cross-clamping has been used for coronary artery bypass grafting before the introduction of hypothermia and cardioplegia. The effects of 60-min sustained vs. intermittent warm ischemias and **reperfusion** was studied in dogs with or without inhibitors of nucleoside transport and **adenosine deaminase**. ATP depletion and nucleoside accumulation and release were measured. The ATP pool is better preserved in intermittent ischemia and **reperfusion** than in sustained ischemia. Nucleoside trapping (by inhibition of nucleoside transport and **adenosine deaminase**) accelerated functional recovery of the stunned myocardium.
ST coronary artery bypass ischemia heart ATP
IT Heart
(aortocoronary bypass surgery, ATP depletion and nucleoside accumulation and release in myocardial stunning and preconditioning during non-cardioplegic warm intermittent aortic cross-clamping)
IT Heart, disease
(ischemia, ATP depletion and nucleoside accumulation and release in myocardial stunning and preconditioning during non-cardioplegic warm intermittent aortic cross-clamping)
IT **Shock**
(**ischemic**, ATP depletion and nucleoside accumulation and release in myocardial stunning and preconditioning during non-cardioplegic warm intermittent aortic cross-clamping)
IT **Perfusion**
(re-, ATP depletion and nucleoside accumulation and release in myocardial stunning and preconditioning during non-cardioplegic warm intermittent aortic cross-clamping)
IT 56-65-5, ATP, biological studies 58-61-7, Adenosine, biological studies 58-63-9, Inosine
RL: BOC (Biological occurrence); BIOL (Biological study); OCCU (Occurrence)
(ATP depletion and nucleoside accumulation and release in myocardial stunning and preconditioning during non-cardioplegic warm intermittent aortic cross-clamping)

L84 ANSWER 7 OF 13 HCAPLUS COPYRIGHT 2002 ACS
AN **1996:283655** HCAPLUS
DN **125:25718**
TI **Pentostatin (2'-deoxycoformycin, dCF**) in patients with low-grade (B-T-cell) and intermediate- and high-grade (T-cell) malignant lymphomas: phase II study of the EORTC early Clinical Trials Group
AU Monfardini, S.; Sorio, R.; Cavalli, F.; Cerny, T.H.; Van Glabbeke, M.; Kaye, S.; Smyth, J.F.
CS Division of Medical Oncology, Centro di Riferimento Oncologico, Aviano, I-33081, Italy
SO Oncology (1996), 53(2), 163-168
CODEN: ONCOBS; ISSN: 0030-2414
DT Journal
LA English
CC 1-6 (Pharmacology)
Section cross-reference(s): 14
AB Thirty-seven eligible patients with advanced non-Hodgkin's lymphoma of

low-grade, T-cell intermediate- and high-grade histol. were treated with **pentostatin** (**2'-deoxycoformycin, dCF**) 4 mg/m2 i.v. weekly for 3 wk and then every 14 days to be followed after 3 doses by the same dosage every 4 wk until max. response or progression. Only patients with no more than two chemotherapy regimens were entered in this trial. All patients had measurable disease, performance status of 1, 0 and 2 and adequate bone marrow, renal and liver function. Five of 37 eligible patients experienced a partial response of 8 mo' median duration (range 7-12). The response rate was 17% in low-grade, 8% in T-cell intermediate- and high-grade and 14% in cutaneous T cell lymphoma. The only eligible patient with Hodgkin's disease underwent progression while on treatment. One case presented with grade 3 leukopenia and another one died of **septicemia**, possibly treatment-related. Elevated but reversible creatinine levels were obsd. in 13% of patients and conjunctivitis in 7%. The toxicity of **dCF** at this low-dose schedule was acceptable, but the therapeutic activity in pretreated patients with low-grade, T-cell intermediate- and high-grade and cutaneous T-cell lymphomas was limited.

ST **pentostatin** non Hodgkin lymphoma inhibitor

IT Lymphoma
(non-Hodgkin's, **pentostatin** in patients with low-grade (B-T-cell) and intermediate- and high-grade (T-cell) malignant lymphomas)

IT Neoplasm inhibitors
(non-Hodgkin's lymphoma, **pentostatin** in patients with low-grade (B-T-cell) and intermediate- and high-grade (T-cell) malignant lymphomas)

IT **9026-93-1, Adenosine deaminase**
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BIOL (Biological study); PROC (Process)
(**pentostatin** in patients with low-grade (B-T-cell) and intermediate- and high-grade (T-cell) malignant lymphomas)

IT **53910-25-1, Pentostatin**
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(**pentostatin** in patients with low-grade (B-T-cell) and intermediate- and high-grade (T-cell) malignant lymphomas)

L84 ANSWER 8 OF 13 HCAPLUS COPYRIGHT 2002 ACS
AN **1996:255993** HCAPLUS
DN **124:332424**
TI **Adenosine deaminase** inhibition prevents **free radical**-mediated injury in the postischemic heart
AU Xia, Yong; Khatchikian, Garabet; Zweier, Jay L.
CS Mol. Cell. Biophys. Lab., Johns Hopkins Bayview Med. Cent., Baltimore, MD, 21224, USA
SO J. Biol. Chem. (1996), 271(17), 10096-102
CODEN: JBCHA3; ISSN: 0021-9258
DT Journal
LA English
CC 1-8 (Pharmacology)
Section cross-reference(s): 14
AB In the presence of its substrates hypoxanthine and xanthine, xanthine oxidase generates oxygen **free radicals** that cause postischemic injury. Recently, it has been demonstrated that the burst of xanthine oxidase-mediated **free radical** generation in the reperfused heart is triggered by a large increase in substrate formation, which occurs secondary to the degrdn. of adenine nucleotides during ischemia. It is now known, however, whether blocking this substrate formation is sufficient to prevent radical generation and functional injury. Therefore, studies were performed in isolated rat hearts in which xanthine oxidase substrate formation was blocked with the

adenosine deaminase inhibitor **erythro-9-(2-hydroxy-3-nonyl) adenine** (**EHNA**), and measurements of contractile function and **free radical** generation were performed. Chromatog. measurements of the intracellular adenine nucleotide pool showed that preischemic administration of **EHNA** blocked postischemic hypoxanthine, xanthine, and inosine formation. ESR spin trapping measurements of **free radical** generation showed that inhibition of **adenosine deaminase** with **EHNA** blocked **free radical** generation and that it also increased the recovery of contractile function by more than 2-fold. Exogenous infusion of hypoxanthine and xanthine totally reversed the protective effects of **EHNA**. These results demonstrate that blockade of xanthine oxidase substrate formation by **adenosine deaminase** inhibition can prevent **free radical** generation and contractile dysfunction in the postischemic heart.

ST **adenosine deaminase** inhibition heart ischemia injury

IT Reactive oxygen species
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(**adenosine deaminase** inhibition prevents **free radical**-mediated injury in the postischemic heart)

IT **Heart, disease**
(injury, **adenosine deaminase** inhibition prevents **free radical**-mediated injury in the postischemic heart)

IT **51350-19-7, erythro-9-(2-Hydroxy-3-nonyl)adenine**
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(**adenosine deaminase** inhibition prevents **free radical**-mediated injury in the postischemic heart)

IT **9026-93-1, Adenosine deaminase**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**adenosine deaminase** inhibition prevents **free radical**-mediated injury in the postischemic heart)

IT 58-63-9, Inosine 68-94-0, Hypoxanthine 69-89-6, Xanthine
RL: MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative)
(**adenosine deaminase** inhibition prevents **free radical**-mediated injury in the postischemic heart)

L84 ANSWER 9 OF 13 HCAPLUS COPYRIGHT 2002 ACS
AN **1994:570562** HCAPLUS
DN **121:170562**
TI **Adenosine deaminase** inhibitors for treatment of the ischemic conditions
IN Gruber, Harry Edward; Erion, Mark David; Firestein, Gary Steven; Young, Mark Alan
PA Gensia, Inc., USA
SO PCT Int. Appl., 31 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K031-70
CC 1-8 (Pharmacology)
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9417809	A1	19940818	WO 1994-US1184	19940202

W: AT, AU, BB, BG, BR, CA, CH, CN, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, LK, LU, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, UZ
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG
AU 9462972 A1 19940829 AU 1994-62972 19940202
PRAI US 1993-14160 19930203
WO 1994-US1184 19940202

AB **Adenosine deaminase** inhibitors are used for treatment of the ischemic conditions. Such conditions include thrombotic conditions, conditions characterized by ischemia and conditions characterized by **inflammatory** responses, including **sepsis**. The IC50 of **2'-deoxycoformycin** in presence of of 10.mu.M adenosine was 0.63.mu.M.

ST **adenosine deaminase** inhibitor ischemic condition treatment; deoxyformycin ischemic condition treatment

IT Burn
Injury
Ischemia
Meningitis
Sepsis and Septicemia
(**adenosine deaminase** inhibitors for treatment of the ischemic conditions)

IT Fungi
Leukocytopenia
Mycobacterium
Surgery
Virus, animal
Worm
Wound
Yeast
(**sepsis** from, **adenosine deaminase** inhibitors for treatment of the ischemic conditions)

IT Respiratory distress syndrome
(adult, **adenosine deaminase** inhibitors for treatment of the ischemic conditions)

IT **Heart, disease**
(angina pectoris, **adenosine deaminase** inhibitors for treatment of the ischemic conditions)

IT **Inflammation** inhibitors
(antiarthritics, **adenosine deaminase** inhibitors for treatment of the ischemic conditions)

IT Antiarteriosclerotics
(antiatherosclerotics, **adenosine deaminase** inhibitors for treatment of the ischemic conditions)

IT **Inflammation** inhibitors
(antirheumatics, **adenosine deaminase** inhibitors for treatment of the ischemic conditions)

IT Therapeutics
(chemo-, **sepsis** from, **adenosine deaminase** inhibitors for treatment of the ischemic conditions)

IT **Sepsis and Septicemia**
(**endotoxemia, adenosine deaminase** inhibitors for treatment of the ischemic conditions)

IT **Shock**
(**endotoxin, adenosine deaminase** inhibitors for treatment of the **ischemic** conditions)

IT Intestine, disease
(enterocolitis, necrotizing; **adenosine deaminase** inhibitors for treatment of the ischemic conditions)

IT Bacteria
(gram-neg., **sepsis** from, **adenosine deaminase** inhibitors for treatment of the ischemic conditions)

IT Bacteria
(gram-pos., **sepsis** from, **adenosine deaminase** inhibitors for treatment of the ischemic conditions)
IT **Heart, disease**
(infarction, **adenosine deaminase** inhibitors for treatment of the ischemic conditions)
IT Intestine, disease
(**inflammatory, adenosine deaminase** inhibitors for treatment of the ischemic conditions)
IT Eye, disease
(iridocyclitis, **adenosine deaminase** inhibitors for treatment of the ischemic conditions)
IT **Blood vessel, disease**
(peripheral, **adenosine deaminase** inhibitors for treatment of the ischemic conditions)
IT **Shock**
(**septic, adenosine deaminase** inhibitors for treatment of the **ischemic** conditions)
IT Brain, disease
(stroke, **adenosine deaminase** inhibitors for treatment of the ischemic conditions)
IT **Shock**
(**toxic shock syndrome, adenosine deaminase** inhibitors for treatment of the **ischemic** conditions)
IT **Blood vessel, disease**
(**vasculitis, adenosine deaminase** inhibitors for treatment of the ischemic conditions)
IT 11033-22-0, Coformycin **51350-19-7, erythro-9-(2-Hydroxy-3-nonyl)adenine 53910-25-1, 2'-Deoxycoformycin**
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(**adenosine deaminase** inhibitors for treatment of the ischemic conditions)
IT **9026-93-1, Adenosine deaminase**
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(inhibitor; **adenosine deaminase** inhibitors for treatment of the ischemic conditions)

L84 ANSWER 10 OF 13 HCAPLUS COPYRIGHT 2002 ACS
AN **1992:411** HCAPLUS
DN **116:411**
TI Host resistance to murine malaria in mice exposed to the **adenosine deaminase** inhibitor, **2'-deoxycoformycin**
AU Luebke, Robert W.; Andrews, Debora L.; Copeland, Carey B.; Riddle, Marie M.; Rogers, Ron R.; Smialowicz, Ralph J.
CS Health Eff. Res. Lab., EPA, Research Triangle Park, NC, USA
SO Int. J. Immunopharmacol. (1991), 13(7), 987-97
CODEN: IJIMDS; ISSN: 0192-0561
DT Journal
LA English
CC 1-7 (Pharmacology)
Section cross-reference(s): 15
AB Resistance to infection with the nonlethal rodent malaria parasite Plasmodium yoelii 7XNL (Py 17XNL) is mediated by humoral, T-cell and accessory cell activity. The purpose of this study was to profile host resistance to infection with this organism in mice exposed to **2'-deoxycoformycin** (**2dCF**), a potent **adenosine deaminase** (ADA) inhibitor. Inhibition of ADA activity by 2dFC results in defective T-cell function and either suppression or augmentation of the humoral response, depending on whether **2dCF**

exposure precedes (suppression) or follows (augmentation) immunization. In this study, mice injected with **2dCF** during the first five days of infection cleared the infection at the same time as controls, but had lower peak **parasitemia** than controls. Mice infected with the lethal variant of P. yoelii were more susceptible to infection when injected with **2dCF** after infection, suggesting that **2dCF** injection did not directly affect the parasite. Rather, suppression of **parasitemia** in **2dCF**-treated mice may have been mediated by augmented humoral immunity, since **2dCF** injection increases antibody responses when **2dCF** injection follows antigen (in this case, parasite) injection. Conversely, in mice given **2dCF** prior to infection, **parasitemia** peaked 2 days later and was eliminated more gradually than in control mice. Exposure to **2dCF** did not deplete reticulocytes and thus temporarily limit **parasitemia**. Similarly, enrichment of NK cells or augmentation of macrophage phagocytic activity prior to infection were not sufficient to alter the pattern of infection. In contrast, the pattern of infection in mice treated with tilorone (a macrophage activator which also causes suppressed T-cell function) prior to infection was similar to that obsd. in **2dCF** -exposed animals. These results indicate that **2dCF**, given before or after infection, alters the host response to infection with Py17XNL. It appears that a contribution of increased macrophage activity and altered T-cell activity contributed to the delay in peak **parasitemia** and clearance at infection in mice exposed to **2dCF** before infection with Py17XNL.

ST malaria resistance **deoxycoformycin** immunity

IT Immunity
(**deoxycoformycin** effect on, host resistance response to malarial infections in relation to)

IT Macrophage
Interferons
RL: BIOL (Biological study)
(**deoxycoformycin** effect on, host resistance to malarial infection in relation to)

IT Malaria
(resistance to, **deoxycoformycin** effect on, mechanism of)

IT Lymphocyte
(T-cell, **deoxycoformycin** effect on, host resistance to malarial infection in relation to)

IT 7773-01-5, Manganese chloride (MnCl2) 27591-69-1 **53910-25-1**
RL: BIOL (Biological study)
(host resistance to malarial infection response to, mechanism of)

L84 ANSWER 11 OF 13 HCAPLUS COPYRIGHT 2002 ACS

AN **1991:490094** HCAPLUS

DN **115:90094**

TI Is adenosine 5'-triphosphate derangement or **free-radical** -mediated injury the major cause of ventricular dysfunction during **reperfusion**? Role of adenine nucleoside transport in myocardial **reperfusion** injury

AU Abd-Elfattah, Anwar S.; Jessen, Michael E.; Hanan, Scott A.; Tuchy, Gert; Wechsler, Andrew S.

CS Dep. Surg., Med. Coll. Virginia, Richmond, VA, 23298-0532, USA

SO Circulation, Suppl. (1990), 82(5), IV341-IV350
CODEN: CISUAQ; ISSN: 0069-4193

DT Journal

LA English

CC 14-5 (Mammalian Pathological Biochemistry)

AB The aim of this study was to det. the dual role of ATP as an energy substrate and as a major source of oxygen-derived **free-radical**-mediated **reperfusion** injury by using adenine nucleoside blocker, p-nitrobenzylthioinosine (NBMPR), and **adenosine deaminase** inhibitor, **erythro-**

9-(2-hydroxy-3-nonyl)
adenine (**EHNA**). In a randomized study, 16 dogs were instrumented with minor-axis LTZ-piezoelec. crystals and intraventricular pressure transducers to monitor, off bypass, left ventricular performance by using a sensitive and load-independent index of contractility (slope of the stroke work-end-diastolic length relation). Hearts were subjected to 60 min of normothermic global ischemia and 120 min of **reperfusion**. Normal saline without (Group 1) or with (Group 2) NBMPR and **EHNA** was infused in three boluses into the cardiopulmonary bypass reservoir before ischemia and **reperfusion**. Normal saline without (Group 1) or with (Group 2) NBMPR and **EHNA** was infused in three boluses into the cardiopulmonary bypass reservoir before ischemia and **reperfusion**. Transmural series biopsies were obtained before and during ischemia and **reperfusion** and analyzed for myocardial adenine nucleotide pool intermediates by using HPLC. In the control group, three hearts developed ischemia contracture and another three hearts exhibited cardiogenic **shock** during **reperfusion**. In the **EHNA**/NBMPR-treated group, left ventricular performance recovered within 30 min of **reperfusion**. Myocardial ATP was depleted to 20% of normal in both groups by the end of ischemia. Intramyocardial adenosine in the **EHNA**/NBMPR-treated group was 12-fold greater than the control group at the end of the ischemia period. Inosine was .apprx.4-fold higher in the control group compared with the drug-treated group. During **reperfusion**, myocardial ATP levels increased to approx. 50% of normal in the **EHNA**/NBMPR group while remaining depressed (20% of normal) in the control group. Thus, despite the dramatic loss of myocardial ATP during ischemia, complete recovery of ventricular performance and significant repletion of ATP during **reperfusion** were obsd. when adenosine transport and deamination were modulated during ischemia and **reperfusion**. These results suggest that (1) the myocardium may have more ATP than is needed for basic cardiac functions and (2) washout of ATP diffusible catabolites is detrimental to ventricular performance during **reperfusion**. Specific blockade of nucleoside transport resulted in complete functional recovery despite low but crit. ATP levels. It is concluded that adenine nucleoside transport regulates the release of **free radical** substrate precursors, thereby preventing ventricular dysfunction during **reperfusion**.

ST ATP heart injury ischemia **reperfusion**

IT **Heart, disease or disorder**
(ischemia, left ventricular dysfunction after **reperfusion** and, ATP role in, oxygen radicals in relation to)

IT **Heart, disease or disorder**
(left ventricle, from ischemia and **reperfusion**, ATP role in, oxygen radicals in relation to)

IT **Perfusion**
(re-, heart ventricle dysfunction after cardiac ischemia and, ATP role in, oxygen radicals in relation to)

IT 7782-44-7D, Oxygen, radicals, biological studies
RL: BIOL (Biological study)
(ATP role in heart left ventricle dysfunction after ischemia and **reperfusion** in relation to)

IT 73-24-5D, 1H-Purin-6-amine, nucleosides
RL: BIOL (Biological study)
(heart left ventricle dysfunction after ischemia and **reperfusion** in relation to)

IT 56-65-5, 5'-ATP, biological studies
RL: BIOL (Biological study)
(in heart left ventricle dysfunction after ischemia and **reperfusion**, oxygen radicals in relation to)

L84 ANSWER 12 OF 13 HCAPLUS COPYRIGHT 2002 ACS
AN **1990:624576** HCAPLUS

DN **113:224576**
TI Method of preventing tissue damage due to ischemia associated with diseases by use of purine nucleoside analogs
IN Gruber, Harry E.
PA University of California, Berkeley, USA
SO U.S., 27 pp. Cont.-in-part of U.S. Ser. No. 845,627.
CODEN: USXXAM
DT Patent
LA English
IC ICM A61K031-70
NCL 514045000
CC 1-8 (Pharmacology)
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 4912092	A	19900327	US 1987-79657	19870729
	EP 623348	A1	19941109	EP 1994-107553	19860408
	R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
	CA 1335716	A1	19950530	CA 1988-573208	19880727
	EP 301900	A2	19890201	EP 1988-307040	19880729
	EP 301900	A3	19890920		
	EP 301900	B1	19960320		
	R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
	WO 8900854	A1	19890209	WO 1988-US2527	19880729
	W: AU, BR, DK, FI, JP, NO				
	AU 8823150	A1	19890301	AU 1988-23150	19880729
	BR 8807151	A	19891017	BR 1988-7151	19880729
	JP 02500916	T2	19900329	JP 1988-506999	19880729
	EP 672418	A2	19950920	EP 1995-102166	19880729
	EP 672418	A3	19960529		
	R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
	AT 135580	E	19960415	AT 1988-307040	19880729
	ES 2087061	T3	19960716	ES 1988-307040	19880729
	FI 8901463	A	19890328	FI 1989-1463	19890328
	DK 8901488	A	19890529	DK 1989-1488	19890328
	NO 8901315	A	19890525	NO 1989-1315	19890329
	US 5030623	A	19910709	US 1989-366167	19890614
	US 5008251	A	19910416	US 1989-401156	19890831
	US 5118601	A	19920602	US 1989-401618	19890831
	AU 9212855	A1	19920604	AU 1992-12855	19920312
	AU 9480393	A1	19950309	AU 1994-80393	19941212
	AU 687112	B2	19980219		

PRAI	US 1984-646785	19840904
	US 1986-845627	19860327
	EP 1986-902696	19860408
	US 1987-79657	19870729
	EP 1988-307040	19880729
	WO 1988-US2527	19880729

AB Purine nucleoside analogs (AICA riboside, 1-.beta.-D-ribofuranosyl-1,2,4-triazole-3-carboxamide, etc.), which can increase the extracellular concn. of adenosine by enhancing the cellular synthesis and release of adenosine, or can stabilize mast cells and inhibit superoxide **free radical** prodn., are used to prevent tissue damage caused by decreased **blood flow** assocd. with diseases (coronary artery occlusion, angina pectoris, diabetes, autism, seizure, arthritis, arrhythmia, **inflammation**, etc.). The purine nucleoside analog can also be used in conjunction with allopurinol, thrombolytic agents (urokinase, coumadin, etc.), inhibitors of nucleoside metab. (succinylaminoimidazole carboxamide riboside, methotrexate, sulfonamides, etc.), catecholamines, or **adenosine deaminase** inhibitors (coformycin, dipyridamole, etc.). Thus, 100-500 .mu.M AICA riboside increased adenosine release by lymphoblasts. Infusion of AICA riboside increased adenosine level as well as myocardial **blood**

flow in dogs. A 33% redn. of myocardial infarct size in rats was produced by AICA riboside treatment. In an autistic patient, two months of continuous AICA riboside administration produced less frequent stereotypic movement and evoked reactions to auditory and tactile stimuli as a clear cut improvement. Pretreatment with 10 .mu.M ribavirin for 3-7 days produced a marked attenuation of mouse mast cell degranulation as measured by .beta.-hexosaminidase release.

ST purine nucleoside analog ischemia prevention; adenosine ischemia tissue damage prevention; nerve tissue damage prevention adenosine; heart tissue damage prevention adenosine; **blood flow** adenosine
ischemia AICA riboside; mast cell degranulation purine nucleoside

IT Sulfonamides
RL: BIOL (Biological study)
(as enhancer of endogenous AICAR, ischemic tissue damage prevention by purine nucleoside analog and)

IT Catecholamines
RL: BIOL (Biological study)
(extracellular adenosine response to purine nucleoside analog and)

IT Thrombolytics
(ischemic tissue damage prevention by purine nucleoside analog and)

IT **Ischemia**
(prevention by purine nucleoside analog)

IT Nerve, disease or disorder
(prevention of ischemic tissue damage in, by increasing extracellular adenosine with purine nucleoside analog)

IT Arthritis
Atherosclerosis
Cerebral palsy
Convulsion
Diabetes mellitus
Epilepsy
Inflammation
Insomnia
Schizophrenia
Thrombosis
(prevention of tissue damage in, by extracellular adenosine enhancement with purine nucleoside analog)

IT Allergy inhibitors
(purine nucleoside analogs, ischemic tissue damage prevention by)

IT Mast cell
(stabilization by purine nucleoside analog)

IT Lymphoblast
(stabilization of degranulation in, by purine nucleoside analog)

IT **Blood vessel, disease or disorder**
(Raynaud's phenomenon, prevention of tissue damage in, by extracellular adenosine enhancement with purine nucleoside analog)

IT Respiratory distress syndrome
(adult, prevention of tissue damage in, by extracellular adenosine enhancement with purine nucleoside analog)

IT **Heart, disease or disorder**
(angina pectoris, prevention of tissue damage in, by extracellular adenosine enhancement with purine nucleoside analog)

IT **Heart, disease or disorder**
(arrhythmia, prevention of tissue damage in, by extracellular adenosine enhancement with purine nucleoside analog)

IT Mental disorder
(autism, prevention of tissue damage in, by extracellular adenosine enhancement with purine nucleoside analog)

IT Disease
(autoimmune, prevention of ischemic tissue damage in, by increasing extracellular adenosine with purine nucleoside analog)

IT **Artery, disease or disorder**
(**coronary, occlusion**, prevention of tissue damage

in, by extracellular adenosine enhancement with purine nucleoside analog)
IT Animal tissue
(disease, ischemia, prevention of, by purine nucleoside analog)
IT Dialysis
(hemo-, prevention of tissue damage in, by extracellular adenosine enhancement with purine nucleoside analog)
IT **Heart, disease or disorder**
(infarction, prevention of, by extracellular adenosine enhancement with purine nucleoside analog)
IT Brain, disease or disorder
Intestine, disease or disorder
Kidney, disease or disorder
Muscle, disease or disorder
Nerve, disease or disorder
Skin, disease or disorder
(ischemia, prevention of, by extracellular adenosine enhancement with purine nucleoside analog)
IT **Blood vessel, disease or disorder**
(**micro-**, ischemic tissue damage prevention of, by extracellular adenosine enhancement with purine nucleoside analog)
IT Headache
(migraine, prevention of tissue damage in, by extracellular adenosine enhancement with purine nucleoside analog)
IT Nerve, disease or disorder
(neuroblastoma, stabilization of degranulation in, by purine nucleoside analog)
IT Eye, disease or disorder
(retina, ischemia, prevention of, by extracellular adenosine enhancement with purine nucleoside analog)
IT **Blood vessel, disease or disorder**
(**spasm**, prevention of tissue damage in, by extracellular adenosine enhancement with purine nucleoside analog)
IT Brain, disease or disorder
(stroke, prevention of tissue damage in, by extracellular adenosine enhancement with purine nucleoside analog)
IT Organ
(transplant, prevention of tissue damage in, by extracellular adenosine enhancement with purine nucleoside analog)
IT 58-32-2, Dipyridamole 11033-22-0, Coformycin **53910-25-1, 2'-Deoxycoformycin 55601-18-8**
RL: BIOL (Biological study)
(as adenosine degrdn. inhibitor, ischemic tissue damage prevention by purine nucleoside analog and)
IT 59-05-2, Methotrexate 3031-95-6, SAICAR 6142-47-8
RL: BIOL (Biological study)
(as enhancer of endogenous AICAR, ischemic tissue damage prevention by purine nucleoside analog and)
IT 2627-69-2, AICAR 36791-04-5, Ribavirin 40925-28-8
RL: BIOL (Biological study)
(as extracellular adenosine enhancer, in ischemic tissue damage prevention)
IT 129-06-6, Coumadin 9002-01-1, Streptokinase 9005-49-6, Heparin, biological studies 9039-53-6, Urokinase
RL: BIOL (Biological study)
(as thrombolytic agent, ischemic tissue damage prevention by purine nucleoside analog and)
IT 9025-10-9, Adenosine monophosphate deaminase
RL: BIOL (Biological study)
(inhibitor as extracellular adenosine enhancer, in ischemic tissue damage prevention)
IT 315-30-0, Allopurinol
RL: BIOL (Biological study)

(ischemic tissue damage prevention by purine nucleoside analog and)
IT 58-61-7, Adenosine, biological studies 58-63-9, Inosine
RL: BIOL (Biological study)
(purine nucleoside analog effect on extracellular, in ischemic tissue damage prevention)
IT 72025-60-6, Leukotriene C4
RL: BIOL (Biological study)
(release of, by mast cell, AICA riboside effect on)
IT 9027-52-5
RL: BIOL (Biological study)
(release of, by mast cell, ribavirin effect on)
IT 105913-11-9, Plasminogen activator
RL: BIOL (Biological study)
(tissue-type, as thrombolytic agent, ischemic tissue damage prevention by purine nucleoside analog and)

L84 ANSWER 13 OF 13 HCAPLUS COPYRIGHT 2002 ACS
AN **1990:584496** HCAPLUS
DN **113:184496**
TI Protective effects of an **adenosine deaminase** inhibitor on ischemia-**reperfusion** injury in isolated perfused rat heart
AU Zhu, Qingyan; Chen, Shanggong; Zou, Cunmei
CS Cardiovasc. Inst., Chin. Acad. Med. Sci., Beijing, 100037, Peop. Rep. China
SO Am. J. Physiol. (1990), 259(3, Pt. 2), H835-H838
CODEN: AJPHAP; ISSN: 0002-9513
DT Journal
LA English
CC 1-8 (Pharmacology)
AB The effect of the **adenosine deaminase** inhibitor **erythro-9-(2-hydroxy-3-nonyl)adenine** (**EHNA**) on ischemia-**reperfusion** injury was studied in isolated perfused rat heart. In the ischemia-**reperfusion** group, ventricular fibrillation occurred within 3 min of **reperfusion** after the 40-min ischemic period. The incidence of ventricular fibrillation was 90% with a mean duration of 3.15 min. Resting tension increased significantly. By contrast, the incidence of ventricular fibrillation after **reperfusion** in the **EHNA**-treated (5 .mu.M) group was 20%, and the duration was 0.30 min. Resting tension was significantly lower and around the normal level in the **EHNA**-treated group. Contraction amplitude and heart rate recovered to nearly normal compared with the ischemia-**reperfusion** group. Coronary flow was greater in the **EHNA**-treated group. It is concluded that **EHNA** protects the heart, possibly by accumulation of adenosine that benefits the hearts and by blocking the xanthine oxidase pathway for **free radical** generation.
ST erythrohydroxynonyladenine heart ischemia **reperfusion** **adenosine deaminase**
IT **Heart, disease or disorder**
(ischemia, injury from **reperfusion** after and, erythrohydroxynonyladenine protection against, as **adenosine deaminase** inhibitor)
IT **9026-93-1, Adenosine deaminase**
RL: BIOL (Biological study)
(erythrohydroxynonyladenine as inhibitor of, heart protection effects of, in ischemia-**reperfusion** injury)
IT **51350-19-7, erythro-9-(2-Hydroxy-3-nonyl)adenine**
RL: PRP (Properties)
(heart protective effects of, in ischemia-**reperfusion** injury, as **adenosine deaminase** inhibitor)

=> fil medline
FILE 'MEDLINE' ENTERED AT 07:58:19 ON 24 JUN 2002

FILE LAST UPDATED: 23 JUN 2002 (20020623/UP). FILE COVERS 1958 TO DATE.

On June 9, 2002, MEDLINE was reloaded. See HELP RLOAD for details.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2002 vocabulary. Enter HELP THESAURUS for details.

THIS FILE CONTAINS CAS REGISTRY NUMBERS FOR EASY AND ACCURATE SUBSTANCE IDENTIFICATION.

=> d all tot

L100 ANSWER 1 OF 10 MEDLINE
AN 2002222392 MEDLINE
DN 21955911 PubMed ID: 11959672
TI Inhibiting **adenosine deaminase** modulates the **systemic inflammatory response syndrome** in **endotoxemia** and **sepsis**.
AU Adanin Simon; Yalovetskiy Igor V; Nardulli Beth A; Sam Albert D 2nd; Jonjev Zivojin S; Law William R
CS Department of Physiology and Biophysics, University of Illinois College of Medicine, Chicago, Illinois 60612, USA.
SO AMERICAN JOURNAL OF PHYSIOLOGY. REGULATORY, INTEGRATIVE AND COMPARATIVE PHYSIOLOGY, (2002 May) 282 (5) R1324-32.
Journal code: 100901230. ISSN: 0363-6119.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200205
ED Entered STN: 20020418
Last Updated on STN: 20020529
Entered Medline: 20020528
AB By pharmacological manipulation of endogenous adenosine, using chemically distinct methods, we tested the hypothesis that endogenous adenosine tempers **proinflammatory** cytokine **responses** and oxyradical-mediated tissue damage during **endotoxemia** and **sepsis**. Rats were pretreated with varying doses of **pentostatin** (PNT; **adenosine deaminase** inhibitor) or 8-sulfophenyltheophylline (8-SPT; adenosine receptor antagonist) and then received either E. coli endotoxin (lipopolysaccharide; 0.01 or 2.0 mg/kg) or a slurry of cecal matter in 5% dextrose in water (200 mg/kg). Resultant levels of tumor necrosis factor (TNF)-alpha, interleukin (IL)-1beta, and IL-10 were measured in serum and in liver and spleen. Untreated, 2 mg/kg lipopolysaccharide elevated serum TNF-alpha, IL-1beta, and IL-10. PNT dose dependently attenuated, without ablating, the elevation in serum TNF-alpha and IL-1beta and raised liver and spleen IL-10. PNT also attenuated elevation of TNF-alpha in serum, liver, and spleen at 4 and 24 h after **sepsis** induction, and 8-SPT resulted in higher **proinflammatory** cytokines. Modulating endogenous adenosine was also effective in exacerbated (8-SPT) or diminished (PNT) tissue peroxidation. Survival from **sepsis** was also improved when PNT was used as a posttreatment. These data indicate that endogenous adenosine is an important modulatory component of **systemic inflammatory response syndromes**. These data also indicate that inhibition of **adenosine deaminase** may be a novel and viable therapeutic approach to managing the **systemic inflammatory response syndrome** without

ablating important physiological functions.
CT Check Tags: Animal; Male; Support, Non-U.S. Gov't
Adenosine Deaminase: AI, antagonists & inhibitors
***Adenosine Deaminase: PH, physiology**
*Bacterial Infections: ME, metabolism
Blood: ME, metabolism
Chronic Disease
***Endotoxemia: ME, metabolism**
Enzyme Inhibitors: PD, pharmacology
Inflammation: ME, metabolism
Interleukin-1: ME, metabolism
Interleukin-10: ME, metabolism
Liver: ME, metabolism
Pentostatin: PD, pharmacology
Peroxides: ME, metabolism
Rats
Rats, Sprague-Dawley
Receptors, Purinergic P1: AI, antagonists & inhibitors
Spleen: ME, metabolism
*Theophylline: AA, analogs & derivatives
Theophylline: PD, pharmacology
Tumor Necrosis Factor: ME, metabolism
RN 130068-27-8 (Interleukin-10); **53910-25-1 (Pentostatin)**; 58-55-9 (Theophylline); 80206-91-3 (8-(4-sulfophenyl)theophylline)
CN 0 (Enzyme Inhibitors); 0 (Interleukin-1); 0 (Peroxides); 0 (Receptors, Purinergic P1); 0 (Tumor Necrosis Factor); **EC 3.5.4.4 (Adenosine Deaminase**
)

L100 ANSWER 2 OF 10 MEDLINE
AN 2001488606 MEDLINE
DN 21421863 PubMed ID: 11531021
TI Inhibition of **adenosine deaminase** attenuates endotoxin-induced release of cytokines in vivo in rats.
AU Tofovic S P; Zacharia L; Carcillo J A; Jackson E K
CS Center for Clinical Pharmacology, University of Pittsburgh School of Medicine, Pennsylvania 15213-2582, USA.
NC HL35909 (NHLBI)
HL55314 (NHLBI)
SO SHOCK, (2001 Sep) 16 (3) 196-202.
Journal code: 9421564. ISSN: 1073-2322.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200203
ED Entered STN: 20010904
Last Updated on STN: 20020319
Entered Medline: 20020318
AB The purpose of this study was to investigate in vivo the effects of modulating the adenosine system on endotoxin-induced release of cytokines and changes in heart performance and neurohumoral status in early, profound **endotoxemia** in rats. Time/pressure variables of heart performance and blood pressure were recorded continuously, and plasma levels of tumor necrosis factor alpha (TNFalpha), interleukin 1-beta (IL-1beta), plasma renin activity (PRA), and catecholamines were determined before and 90 min after administration of endotoxin (30 mg/kg of lipopolysaccharide, i.v.). **Erythro-9[2-hydroxyl-3-nonyl] adenine** (**EHNA**; an **adenosine deaminase** inhibitor) had no effects on measured time-pressure variables of heart performance under baseline conditions and during **endotoxemia**, yet significantly attenuated endotoxin-induced release of cytokines and PRA. Pretreatment

with the non-selective adenosine receptor antagonist DPSPX not only prevented the effects of **EHNA** but also increased the basal release of cytokines and augmented PRA. At baseline, caffeine (a non-selective adenosine receptor antagonist) increased HR, +dP/dtmax, heart rate x ventricular pressure product (HR x VPSP) and +dP/dtmax normalized by pressure (+dP/dtmax/VPSP), and these changes persisted during **endotoxemia**. Caffeine attenuated endotoxin-induced release of cytokines and augmented endotoxin-induced increases in plasma catecholamines and PRA. Pretreatment with propranolol abolished the effects of caffeine on heart performance and neurohumoral activation during the early phase of **endotoxemia**. 6N-cyclopentyladenosine (CPA; selective A1 adenosine receptor agonist) induced bradicardia and negative inotropic effects, reduced work load (i.e., decreased HR, VPSP, +dP/dtmax, +dP/dtmax/VPSP and HR x VPSP) and inhibited endotoxin-induced tachycardia and renin release. CGS 21680 (selective A2A adenosine receptor agonist) decreased blood pressure under basal condition but did not potentiate decreases in blood pressure during **endotoxemia**. CGS 21680 completely inhibited endotoxin-induced release of TNFalpha, augmented sympathetic activity and PRA, and increased +dP/dtmax and +dP/dtmax/VPSP in the absence and presence of endotoxin. The present study provides strong evidence that inhibition of **adenosine deaminase** reduces cytokine release in vivo without producing significant hemodynamic and cardiac effects during the early phase of profound **endotoxemia** in rats. The augmented neurohumoral activation induced by caffeine is associated with decreased cytokine release induced by endotoxin. Further studies are warranted to determine the impact of these effects on cardiac function and hemodynamics in the late phase of **endotoxemia**.

CT Check Tags: Animal; Male; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
*Adenine: AA, analogs & derivatives
Adenine: PD, pharmacology
Adenosine: ME, metabolism
Adenosine Deaminase: AI, antagonists & inhibitors
***Adenosine Deaminase: ME, metabolism**
Blood Pressure: DE, drug effects
Caffeine: PD, pharmacology
Catecholamines: BL, blood
*Cytokines: ME, metabolism
Endotoxemia: DT, drug therapy
Endotoxemia: ME, metabolism
***Endotoxemia: PP, physiopathology**
Endotoxins: TO, toxicity
Enzyme Inhibitors: PD, pharmacology
Heart: DE, drug effects
*Heart: PP, physiopathology
Heart Rate: DE, drug effects
Propranolol: PD, pharmacology
Rats
Rats, Sprague-Dawley
Receptors, Purinergic P1: AI, antagonists & inhibitors
Renin: BL, blood
Xanthines: PD, pharmacology

RN 525-66-6 (Propranolol); 58-08-2 (Caffeine); 58-61-7 (Adenosine); **59262-86-1 (9-(2-hydroxy-3-nonyl)adenine)**; 73-24-5 (Adenine); 89073-57-4 (1,3-dipropyl-8-(4-sulfophenyl)xanthine)

CN 0 (Catecholamines); 0 (Cytokines); 0 (Endotoxins); 0 (Enzyme Inhibitors); 0 (Receptors, Purinergic P1); 0 (Xanthines); EC 3.4.23.15 (Renin); **EC 3.5.4.4** (**Adenosine Deaminase**)

L100 ANSWER 3 OF 10 MEDLINE
AN 96202551 MEDLINE

DN 96202551 PubMed ID: 8619186
TI Acadesine and lipopolysaccharide-evoked pulmonary dysfunction after resuscitation from traumatic shock.
AU Fabian T C; Fabian M J; Yockey J M; Proctor K G
CS Department of Surgery, University of Tennessee Health Science Center, Memphis 38163, USA.
SO SURGERY, (1996 Mar) 119 (3) 302-15.
Journal code: 0417347. ISSN: 0039-6060.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 199606
ED Entered STN: 19960620
Last Updated on STN: 19960620
Entered Medline: 19960610
AB BACKGROUND: We have reported that the purine precursor acadesine (AICAR) improved the microcirculation, repleted adenosine triphosphate, and attenuated local and lung neutrophil infiltration after intestinal reperfusion and that it quickly improved systemic hemodynamics after resuscitation from hemorrhagic shock. This study evaluated the therapeutic potential of AICAR after fluid resuscitated trauma. METHODS: Anesthetized (fentanyl) mongrel pigs were subjected to tissue injury plus hemorrhage and randomized to receive resuscitation fluids comprised of shed blood plus either lactated Ringer's solution (LR) or AICAR (1 or 10 mg/kg bolus + 0.5 mg/kg/min x 30 min). Thereafter either LR or AICAR (1 or 10 mg/kg) was administered at 12-hour intervals for 72 hours. In a smaller series (n = 7) a single bolus (0.5 mg/kg) of the **adenosine deaminase** inhibitor **deoxycoformycin** was administered at the time of resuscitation. After 72 hours, and endotoxin challenge (0.5 microgram/kg, lipopolysaccharide [LPS]) was administered. RESULTS: At 1 mg/kg (n = 9), AICAR had no obvious effect versus LR (n = 31). At 10 mg/kg AICAR (n = 11), the fluid required to stabilize hemodynamics after trauma was higher (66 +/- 5 versus 52 +/- 3 ml/kg/hr, p = 0.014), but there were fewer deaths 3 days after trauma versus LR (0 of 11 versus 4 of 31, p = 0.210), fewer deaths within 5 hours after LPS administration (3 of 11 versus 16 of 27, p = 0.074), and a longer survival time after LPS administration (4.5 +/- 0.3 versus 3.9 +/- 0.2 hr, p = 0.054). **Deoxycoformycin** had similar salutary effects on survival after LPS administration. LPS increased protein permeability of pulmonary capillaries, increased peak inspiratory pressures on constant tidal volume, increased dead space ventilation, and caused progressive arterial desaturation on 0.65 FiO2 (all $p < 0.05$). This pulmonary dysfunction was associated with a compensatory increase in cardiac output, decrease in systemic vascular resistance, increase in O2 consumption, and rise in plasma cortisol level (all $p < 0.05$). All these changes were blunted or eliminated with 10 mg/kg AICAR. Hematocrit and systemic pressures were maintained relatively constant after LPS administration with fluid resuscitation, but less was required with AICAR versus LR (40 +/- 8 versus 83 +/- 14 ml/kg/hr, p = 0.023). AICAR caused a concentration-related reduction in CD18 expression on LPS-stimulated neutrophils in vitro, but there was no effect versus LR on circulating leukocyte counts in vivo and no effect of AICAR on LPS-stimulated production of tumor necrosis factor in vitro or in vivo. CONCLUSIONS: 1. AICAR reduced the pulmonary dysfunction associated with posttrauma **endotoxemia** but had no effect on circulating leukocytes, so its mechanism could be related to an adenosine-mediated improvement in peripheral perfusion or O2 use. 2. AICAR is a generic compound that is safe and apparently efficacious in human beings, so AICAR prophylaxis could be cost-effectively administered to trauma patients.
CT Check Tags: Animal; Support, Non-U.S. Gov't
Adenosine: PH, physiology
*Aminoimidazole Carboxamide: AA, analogs & derivatives

Aminoimidazole Carboxamide: PD, pharmacology
Capillary Permeability: DE, drug effects
Hydrocortisone: BL, blood
Leukocyte Count
*Lipopolysaccharides: TO, toxicity
*Lung: DE, drug effects
*Resuscitation
*Ribonucleosides: PD, pharmacology
*Shock, Traumatic: PP, physiopathology
Swine
Tumor Necrosis Factor: BI, biosynthesis
RN 2627-69-2 (acadesine); 360-97-4 (Aminoimidazole Carboxamide); 50-23-7 (Hydrocortisone); 58-61-7 (Adenosine)
CN 0 (Lipopolysaccharides); 0 (Ribonucleosides); 0 (Tumor Necrosis Factor)

L100 ANSWER 4 OF 10 MEDLINE
AN 93319187 MEDLINE
DN 93319187 PubMed ID: 8101069
TI Complete remissions in hairy cell leukemia with 2-chlorodeoxyadenosine after failure with **2'-deoxycoformycin**.
CM Comment in: Ann Intern Med. 1994 Feb 1;120(3):247-8
Comment in: Ann Intern Med. 1994 Jan 15;120(2):169
AU Saven A; Piro L D
CS Scripps Clinic and Research Foundation, La Jolla, California.
SO ANNALS OF INTERNAL MEDICINE, (1993 Aug 15) 119 (4) 278-83.
Journal code: 0372351. ISSN: 0003-4819.
CY United States
DT (CLINICAL TRIAL)
(CLINICAL TRIAL, PHASE II)
Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 199308
ED Entered STN: 19930820
Last Updated on STN: 19950206
Entered Medline: 19930812
AB OBJECTIVE: To determine whether clinical cross-resistance and intolerance exists between the nucleosides **2'-deoxycoformycin** (**DCF**) and 2-chlorodeoxyadenosine (2-CdA) in the treatment of patients with hairy cell leukemia despite similar structures and mechanisms of action. DESIGN: Phase II clinical study. SETTING: Referral cancer center. PARTICIPANTS: Five patients with hairy cell leukemia who had been previously treated with **DCF**. INTERVENTION: Single course of 2-CdA at 0.1 mg/kg body weight per day for 7 days by continuous intravenous infusion. RESULTS: Of five patients, three were resistant to and two were intolerant of (having had life-threatening toxic reactions) **DCF** therapy. Four patients obtained a complete response with a median follow-up period of more than 11 months. The other patient in whom splenectomy, interferon, and **DCF** treatments were unsuccessful had a partial response lasting 2 months and subsequently died of Streptococcus pneumoniae **bacteremia**. Three of the four patients with complete responses remain in unmaintained remission, whereas the fourth has progressive splenic enlargement with stable hematologic parameters. The median leukocyte count increased from 2.0 x 10(9)/L to 3.8 x 10(9)/L, the median absolute neutrophil count increased from 0.56 x 10(9)/L to 2.73 x 10(9)/L, the median hemoglobin level increased from 112 g/L to 140 g/L, and the median platelet count increased from 55 x 10(9)/L to 123 x 10(9)/L. Two patients had culture-negative neutropenic fever associated with treatment. CONCLUSIONS: 2-Chlorodeoxyadenosine induced complete responses in patients with hairy cell leukemia resistant to **DCF**, suggesting a lack of cross-resistance. Also, 2-CdA is not prohibitively toxic in patients intolerant of **DCF**.
CT Check Tags: Female; Human; Male

Adult
Cladribine: AE, adverse effects
*Cladribine: TU, therapeutic use
Drug Resistance
Hematologic Tests
Immunophenotyping
Leukemia, Hairy Cell: BL, blood
*Leukemia, Hairy Cell: DT, drug therapy
Lymphocyte Subsets: DE, drug effects
Middle Age
Pentostatin: TU, therapeutic use
Remission Induction
RN 4291-63-8 (Cladribine); **53910-25-1 (Pentostatin)**

L100 ANSWER 5 OF 10 MEDLINE
AN 93136044 MEDLINE
DN 93136044 PubMed ID: 1283078
TI Massive abdominal lymphadenopathy in hairy cell leukaemia: a report of 12 cases.
AU Mercieca J; Matutes E; Moskovic E; MacLennan K; Matthey F; Costello C; Behrens J; Basu S; Roath S; Fairhead S; +
CS Department of Academic Haematology and Cytogenetics, Royal Marsden Hospital, London.
SO BRITISH JOURNAL OF HAEMATOLOGY, (1992 Nov) 82 (3) 547-54.
Journal code: 0372544. ISSN: 0007-1048.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199302
ED Entered STN: 19930312
Last Updated on STN: 19960129
Entered Medline: 19930219
AB Lymphadenopathy is an uncommon finding in hairy cell leukaemia (HCL). We report 12 HCL patients in whom relapse was associated with massive abdominal lymphadenopathy. All but one had long-standing HCL (range 3-25 years; median 10 years); in one it was discovered at presentation. Nine patients had been splenectomized and seven had previously been treated with **2'deoxycoformycin** (**DCF**) and/or alpha-interferon (alpha IFN): three had achieved complete remission and four a partial response. The computerized tomography (CT) scan appearances were similar in all cases with a primary lymph node mass centred around the coeliac axis and involving upper para-aortic and retropancreatic regions. Histology and/or cytology confirmed nodal involvement by HCL in six patients. Large immature hairy cells were seen in both lymph nodes and bone marrow, suggesting a degree of transformation. Nine patients were treated with **DCF**: one had complete resolution, six responded with 50-90% reduction of the lymphadenopathy, one did not respond and one is still on treatment; alpha-IFN was used concomitantly or sequentially in two of the responders. One responding patient died of **sepsis** after four injections of **DCF**. Three patients received either alpha- or beta-IFN alone with no response. One elderly patient was not treated. Abdominal lymphadenopathy could be part of the natural history of HCL and/or may represent a transformation analogous to that seen in other low-grade lymphoproliferative disorders. Routine abdominal CT scanning should be part of the work up of all patients with HCL.
CT Check Tags: Case Report; Female; Human; Male; Support, Non-U.S. Gov't
Adult
Aged
Interferons: TU, therapeutic use
*Leukemia, Hairy Cell: CO, complications
Leukemia, Hairy Cell: PA, pathology
Leukemia, Hairy Cell: RA, radiography

*Lymphatic Diseases: ET, etiology
Lymphatic Diseases: PA, pathology
Lymphatic Diseases: RA, radiography
Middle Age
Pentostatin: TU, therapeutic use
Radiography, Abdominal
Tomography, X-Ray Computed
RN **53910-25-1 (Pentostatin)**; 9008-11-1 (Interferons)

L100 ANSWER 6 OF 10 MEDLINE
AN 93085392 MEDLINE
DN 93085392 PubMed ID: 1453206
TI Phase II study of **pentostatin** and intermittent high-dose recombinant interferon alfa-2a in advanced mycosis fungoides/Sezary syndrome.
AU Foss F M; Ihde D C; Breneman D L; Phelps R M; Fischmann A B; Schechter G P; Linnoila I; Breneman J C; Cotelingam J D; Ghosh B C; +
CS National Cancer Institute, National Institutes of Health, Bethesda, MD.
SO JOURNAL OF CLINICAL ONCOLOGY, (1992 Dec) 10 (12) 1907-13.
Journal code: 8309333. ISSN: 0732-183X.
CY United States
DT (CLINICAL TRIAL)
(CLINICAL TRIAL, PHASE II)
Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199301
ED Entered STN: 19930129
Last Updated on STN: 19930129
Entered Medline: 19930107
AB PURPOSE: This phase II study was undertaken to assess the efficacy and toxicity of alternating administration of **pentostatin** (**deoxycoformycin [DCF]**) and interferon alfa-2a (IFN) in patients with advanced or refractory mycosis fungoides (MF) or the Sezary syndrome (SS). PATIENTS AND METHODS: Forty-one patients underwent therapy with alternating cycles of **DCF** 4 mg/m2 intravenously (IV) days 1 through 3 and IFN 10 million U/m2 intramuscularly (IM) day 22, and 50 million U/m2 intramuscularly (IM) days 23 through 26. Twenty-nine patients had not responded to prior chemotherapy or total-skin electron-beam irradiation (TSEB), six had not responded to topical therapies, and six had no previous treatment. RESULTS: Two patients achieved a complete response (CR) and 15 achieved a partial response (PR), for an overall response rate of 41% (95% confidence interval, 26% to 58%). No responses were observed in the seven patients with visceral involvement. The median progression-free survival of patients who responded was 13.1 months. IFN-related constitutional symptoms were reported in 39% of patients; severe toxicities included cardiomyopathy in one patient, acute and chronic pulmonary dysfunction in four, and reversible mental status changes in two. Seven patients developed herpes zoster during therapy and six had staphylococcal **bacteremia**. CONCLUSION: These results suggest that the combination of **DCF** and IFN is an active regimen in MF patients without visceral involvement.
CT Check Tags: Female; Human; Male
Adult
Antineoplastic Combined Chemotherapy Protocols: AE, adverse effects
*Antineoplastic Combined Chemotherapy Protocols: TU, therapeutic use
Interferon Alfa-2a: AD, administration & dosage
Middle Age
*Mycosis Fungoides: DT, drug therapy
Mycosis Fungoides: PA, pathology
Neoplasm Staging
Pentostatin: AD, administration & dosage
*Sezary Syndrome: DT, drug therapy

Sezary Syndrome: PA, pathology
*Skin Neoplasms: DT, drug therapy
Skin Neoplasms: PA, pathology
Survival Analysis
Treatment Outcome
RN **53910-25-1 (Pentostatin)**; 76543-88-9 (Interferon Alfa-2a)
CN 0 (Antineoplastic Combined Chemotherapy Protocols)

L100 ANSWER 7 OF 10 MEDLINE
AN 92144989 MEDLINE
DN 92144989 PubMed ID: 1346577
TI Treatment of hairy cell leukemia with 2-chlorodeoxyadenosine (2-CdA).
AU Estey E H; Kurzrock R; Kantarjian H M; O'Brien S M; McCredie K B; Beran M; Koller C; Keating M J; Hirsch-Ginsberg C; Huh Y O; +
CS Department of Hematology, University of Texas M.D. Anderson Cancer Center, Houston 77030.
SO BLOOD, (1992 Feb 15) 79 (4) 882-7.
Journal code: 7603509. ISSN: 0006-4971.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 199203
ED Entered STN: 19920405
Last Updated on STN: 19950206
Entered Medline: 19920316
AB We administered one course of 2-chlorodeoxyadenosine (2CdA) at 4 mg/m2 daily for 7 days by continuous intravenous infusion to 46 patients with hairy cell leukemia. Complete remissions occurred in 36 patients (78%; 95% confidence limits, 63% to 89%), partial remissions in five (11%), and a minor response in one. One patient died of candida **sepsis** 3 weeks after beginning treatment and three patients were clearly resistant to therapy. These three either had morphologically atypical hairy cells, less than 20% of which expressed Ig light chain on the cell surface, or had failed prior treatment with **deoxycoformycin** and interferon-alpha. At a median of 37 weeks since discontinuation of therapy, recurrent thrombocytopenia has developed in one patient, whose marrow remains normal, while a bone marrow relapse has occurred in another patient, whose blood counts remain normal. Treatment produced a greater than 50% decrease in neutrophil count in 26 patients, which lasted 3 to 4 weeks and was associated with an increased incidence of febrile episodes. These episodes occurred in 21 patients but were associated with documented infection in only four patients. Decreases in the number of CD4+ lymphocytes appeared to occur regularly after treatment and have persisted for a median of 18 weeks without obvious clinical significance. Although years of follow-up will be needed, our results confirm Piro et al's observation (N Engl J Med 322: 1117, 1990) that 2CdA appears to be highly effective in the treatment of hairy cell leukemia.
CT Check Tags: Human; Male
2-Chloroadenosine: AD, administration & dosage
2-Chloroadenosine: AE, adverse effects
*2-Chloroadenosine: AA, analogs & derivatives
2-Chloroadenosine: TU, therapeutic use
*Antineoplastic Agents: TU, therapeutic use
Cladribine
Deoxyadenosines: AD, administration & dosage
Deoxyadenosines: AE, adverse effects
*Deoxyadenosines: TU, therapeutic use
Drug Resistance
*Leukemia, Hairy Cell: DT, drug therapy
Leukemia, Hairy Cell: PA, pathology
Leukocyte Count
Leukopenia: CI, chemically induced

Middle Age
Neutrophils: PA, pathology
Platelet Count
Remission Induction
T-Lymphocytes, Helper-Inducer: PA, pathology
T-Lymphocytes, Suppressor-Effector: PA, pathology
RN 146-77-0 (2-Chloroadenosine); 4291-63-8 (Cladribine)
CN 0 (Antineoplastic Agents); 0 (Deoxyadenosines)

L100 ANSWER 8 OF 10 MEDLINE
AN 92104765 MEDLINE
DN 92104765 PubMed ID: 1761363
TI Host resistance to murine malaria in mice exposed to the **adenosine deaminase** inhibitor, **2'-deoxycoformycin.**
AU Luebke R W; Andrews D L; Copeland C B; Riddle M M; Rogers R R; Smialowicz R J
CS Health Effects Research Laboratory, U.S. EPA, Research Triangle Park, North Carolina.
SO INTERNATIONAL JOURNAL OF IMMUNOPHARMACOLOGY, (1991) 13 (7) 987-97. Journal code: 7904799. ISSN: 0192-0561.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199202
ED Entered STN: 19920302
Last Updated on STN: 19970203
Entered Medline: 19920207
AB Resistance to infection with the nonlethal rodent malaria parasite Plasmodium yoelii 17XNL (Py 17XNL) is mediated by humoral, T-cell and accessory cell activity. The purpose this study was to profile host resistance to infection with this organism in mice exposed to **2'-deoxycoformycin** (**2dCF**), a potent **adenosine deaminase** (ADA) inhibitor. Inhibition of ADA activity by 2dFC results in defective T-cell function and either suppression or augmentation of the humoral response, depending on whether **2dCF** exposure precedes (suppression) or follows (augmentation) immunization. In this study, mice injected with **2dCF** during the first five days of infection cleared the infection at the same time as controls, but had lower peak **parasitemia** than controls. Mice infected with the lethal variant of P. yoelii were more susceptible to infection when injected with **2dCF** after infection, suggesting that **2dCF** injection did not directly affect the parasite. Rather, suppression of **parasitemia** in **2dCF**-treated mice may have been mediated by augmented humoral immunity, since **2dCF** injection increases antibody responses when **2dCF** injection follows antigen (in this case, parasite) injection. Conversely, in mice given **2dCF** prior to infection, **parasitemia** peaked 2 days later and was eliminated more gradually than in control mice. Exposure to **2dCF** did not deplete reticulocytes and thus temporarily limit **parasitemia.** Similarly, enrichment of NK cells or augmentation of macrophage phagocytic activity prior to infection were not sufficient to alter the pattern of infection. In contrast, the pattern of infection in mice treated with tilorone (a macrophage activator which also causes suppressed T-cell function) prior to infection was similar to that observed in **2dCF** -exposed animals. These results indicate that **2dCF**, given before or after infection, alters the host response to infection with Py17XNL. It appears that a combination of increased macrophage activity and altered T-cell activity contributed to the delay in peak **parasitemia** and clearance of infection in mice exposed to **2dCF** before infection with Py17XNL.
CT Check Tags: Animal; Female
Adenosine Deaminase: AI, antagonists & inhibitors

Macrophages: DE, drug effects
Macrophages: IM, immunology
*Malaria: DT, drug therapy
Malaria: IM, immunology
Malaria: PS, parasitology
Manganese: PD, pharmacology
Mice
Mice, Inbred C57BL
***Pentostatin: PD, pharmacology**
*Plasmodium yoelii
T-Lymphocytes: DE, drug effects
T-Lymphocytes: IM, immunology
Tilorone: PD, pharmacology
Time Factors
RN 27591-97-5 (Tilorone); **53910-25-1 (Pentostatin)**; 7439-96-5 (Manganese); 7773-01-5 (manganese chloride)
CN **EC 3.5.4.4** (**Adenosine Deaminase**)

L100 ANSWER 9 OF 10 MEDLINE
AN 88052443 MEDLINE
DN 88052443 PubMed ID: 2890428
TI **2'-Deoxycoformycin** therapy in adult T-cell leukemia/lymphoma.
AU Lofters W; Campbell M; Gibbs W N; Cheson B D
CS University of the West Indies, Kingston, Jamaica.
NC N01-CP-31006 (NCI)
SO CANCER, (1987 Dec 1) 60 (11) 2605-8.
Journal code: 0374236. ISSN: 0008-543X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals; AIDS
EM 198712
ED Entered STN: 19900305
Last Updated on STN: 19970203
Entered Medline: 19871221
AB Six Caribbean patients with histologically and immunologically characterized adult T-cell leukemia/lymphoma (ATL) were treated intravenously (IV) with **2'-deoxycoformycin** (**DCF**) at a dose of 5 mg/m2 on days 1, 2, 8, 15, and 22 with four additional weekly doses to convert any partial responses (PR) to complete responses (CR). Patients were considered eligible for this study if refractory to or relapsed from combination chemotherapy, had a life expectancy of 4 weeks or more, a performance status greater than or equal to 50%, normal renal and hepatic function, and no chemotherapy within 4 weeks. Clinical characteristics of the patients in this study included lymphadenopathy in five patients, skin involvement in four patients, bone marrow infiltration in five patients, and central nervous system involvement in two patients. Circulating ATL cells were present in four patients, and three were hypercalcemic. Of five patients evaluable for response, there was one PR of 1 month, and two minor responses lasting 2 and 3 weeks. The median duration of survival for all treated patients was 3 weeks or more. The **DCF** was associated with moderate side effects, including conjunctivitis in three patients, nausea and vomiting in two patients, progressive hepatic insufficiency in one patient, and moderate myelotoxicity in three patients. Infections occurred in four patients, including two cases of oral candidiasis and two cases of fatal neutropenic **sepsis** in patients receiving concurrent intrathecal methotrexate. As a single agent, **DCF** appears to have limited activity in advanced refractory/relapsed ATL. Studies in the future should explore **DCF** in combination with other cytotoxic agents as initial therapy in better-risk patients.

CT Check Tags: Female; Human; Male; Support, U.S. Gov't, P.H.S.
Adult
Aged
Coformycin: AE, adverse effects
Coformycin: AA, analogs & derivatives
*Coformycin: TU, therapeutic use
Deltaretrovirus Infections: BL, blood
*Deltaretrovirus Infections: DT, drug therapy
Deltaretrovirus Infections: MO, mortality
Drug Evaluation
Pentostatin
*Ribonucleosides: TU, therapeutic use
RN 11033-22-0 (Coformycin); **53910-25-1 (Pentostatin)**
CN 0 (Ribonucleosides)

L100 ANSWER 10 OF 10 MEDLINE
AN 84111607 MEDLINE
DN 84111607 PubMed ID: 6363411
TI Human malaria parasite **adenosine deaminase**.
Characterization in host enzyme-deficient erythrocyte culture.
AU Daddona P E; Wiesmann W P; Lambros C; Kelley W N; Webster H K
NC RO1-AM 19045 (NIADDK)
RO1-CA 26284 (NCI)
SO JOURNAL OF BIOLOGICAL CHEMISTRY, (1984 Feb 10) 259 (3) 1472-5.
Journal code: 2985121R. ISSN: 0021-9258.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 198403
ED Entered STN: 19900319
Last Updated on STN: 19970203
Entered Medline: 19840316
AB Human malaria infected erythrocytes show a dramatic increase in **adenosine deaminase** activity in vitro. Using recently developed culture techniques, **adenosine deaminase** -deficient human erythrocytes were infected in vitro with the major human pathogen Plasmodium falciparum. **Adenosine deaminase** activity was undetectable in the uninfected host red cells, but increased by 2-fold over normal levels in these cells with an 8% **parasitemia** . The enzyme in these cells appeared unique in that its activity was markedly elevated over that of other parasite purine enzymes, was not cross-reactive with antibody against human erythrocyte **adenosine deaminase**, and though inhibited competitively by **deoxycoformycin** was relatively insensitive to **erythro-9-(2-hydroxy-3-nonyl) adenine**. The use of **adenosine deaminase** -deficient erythrocytes for the in vitro cultivation of Plasmodium provides a unique system for the study of parasite enzyme and allows further insight into the purine metabolism of the intraerythrocytic malaria parasite.
CT Check Tags: Animal; Human; Support, U.S. Gov't, P.H.S.
Adenosine Deaminase: DF, deficiency
Adenosine Deaminase: IP, isolation & purification
***Adenosine Deaminase: ME, metabolism**
Coformycin: AA, analogs & derivatives
Coformycin: PD, pharmacology
*Erythrocytes: PH, physiology
Immunosuppressive Agents: PD, pharmacology
Kinetics
*Nucleoside Deaminases: ME, metabolism
Pentostatin
*Plasmodium falciparum: EN, enzymology

RN 11033-22-0 (Coformycin); **53910-25-1 (Pentostatin)**
CN 0 (Immunosuppressive Agents); EC 3.5.4 (Nucleoside Deaminases); **EC 3.5.4.4 (Adenosine Deaminase)**

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L108 ANSWER 1 OF 1 EMBASE
AN 93064202 EMBASE
DN **1993064202**
TI Phase II study of **pentostatin** and intermittent high-dose recombinant interferon alfa-2a in advanced mycosis fungoides/Sezary syndrome.
AU Foss F.M.; Ihde D.C.; Breneman D.L.; Phelps R.M.; Fischmann A.B.; Schechter G.P.; Linnoila I.; Breneman J.C.; Cotelingam J.D.; Ghosh B.C.; Steinberg S.M.; Lynch J.W.; Phares J.C.; Stocker J.L.; Bastian A.; Sausville E.A.
CS Boston University Medical Center, Evans 556, 88 E Newton St,Boston, MA 02118, United States
SO Journal of Clinical Oncology, (1992) 10/12 (1907-1913).
ISSN: 0732-183X CODEN: JCONDN
CY United States
DT Journal; Article
FS 013 Dermatology and Venereology
016 Cancer
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LA English
SL English
AB Purpose: This phase II study was undertaken to assess the efficacy and toxicity of alternating administration of **pentostatin** (**deoxycoformycin** [**DCF**]) and interferon alfa-2a (IFN) in patients with advanced or refractory mycosis fungoides (MF) or the Sezary syndrome (SS). Patients and Methods: Forty-one patients underwent therapy with alternating cycles of **DCF** 4 mg/m2 intravenously (IV) days 1 through 3 and IFN 10 million U/m2 intramuscularly (IM) day 22, and 50 million U/m2 intramuscularly (IM) days 23 through 26. Twenty-nine patients had not responded to prior chemotherapy or total-skin electron-beam irradiation (TSEB), six had not responded to topical therapies, and six had no previous treatment. Results: Two patients achieved a complete response (CR) and 15 achieved a partial response (PR), for an overall response rate of 41% (95% confidence interval, 26% to 58%). No responses were observed in the seven patients with visceral involvement. The median progression-free survival of patients who responded was 13.1 months. IFN-related constitutional symptoms were reported in 39% of patients; severe toxicities included cardiomyopathy in one patient, acute and chronic pulmonary dysfunction in four, and reversible mental status changes in two. Seven patients developed herpes zoster during therapy and six had staphylococcal **bacteremia**. Conclusion: These results suggest that the combination of **DCF** and IFN is an active regimen in MF

patients without visceral involvement.
CT Medical Descriptors:
*cancer chemotherapy
*phase 2 clinical trial
*sezary syndrome: DT, drug therapy
article
cardiomyopathy: SI, side effect
clinical article
drug intermittent therapy
drug megadose
female
herpes zoster: CO, complication
human
intramuscular drug administration
intravenous drug administration
lung disease: SI, side effect
male
mental disease: SI, side effect
priority journal
staphylococcus infection: CO, complication
Drug Descriptors:
***pentostatin: AE, adverse drug reaction**
***pentostatin: CT, clinical trial**
***pentostatin: CB, drug combination**
***pentostatin: DT, drug therapy**
*recombinant alpha2a interferon: AE, adverse drug reaction
*recombinant alpha2a interferon: CT, clinical trial
*recombinant alpha2a interferon: CB, drug combination
*recombinant alpha2a interferon: DO, drug dose
*recombinant alpha2a interferon: DT, drug therapy
RN (**pentostatin**) **53910-25-1**

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L143 ANSWER 1 OF 6 WPIX (C) 2002 THOMSON DERWENT
AN 2001-168503 [17] WPIX
DNC C2001-050332
TI Use of an anti-**adenosine deaminase** agent such as

pentastatin, for treating autoimmune disease, e.g. multiple sclerosis, systemic lupus erythematosus, diabetes, meningitis, scleroderma or glomerulonephritis.

DC B05
IN DANG, N H; ENNS, T
PA (SUPE-N) SUPERGEN INC
CYC 95
PI WO 2001007054 A1 20010201 (200117)* EN 25p A61K031-7076
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2000062340 A 20010213 (200128) A61K031-7076
EP 1200102 A1 20020502 (200236) EN A61K031-7076
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
ADT WO 2001007054 A1 WO 2000-US20081 20000721; AU 2000062340 A AU 2000-62340 20000721; EP 1200102 A1 EP 2000-948911 20000721, WO 2000-US20081 20000721
FDT AU 2000062340 A Based on WO 200107054; EP 1200102 A1 Based on WO 200107054
PRAI US 2000-620254 20000720; US 1999-145365P 19990722
IC ICM A61K031-7076
ICS A61K031-00; A61K031-7056; A61K045-06; A61P037-00; A61P037-06
AB WO 200107054 A UPAB: 20010328
NOVELTY - A novel method for treating an autoimmune disease comprises administering to a patient an anti-**adenosine deaminase** (ADA) agent.

ACTIVITY - Immunosuppressive; neuroprotective; antithyroid; dermatological; antiinflammatory; antidiabetic; antibacterial; nephrotropic; antiarthritic; antirheumatic. No tests for the activity of the agent is given.

MECHANISM OF ACTION - Inhibitors of ADA-mediated T lymphocyte activation.

USE - The methods can be used for treating autoimmune diseases such as multiple sclerosis, Graves' disease, systemic lupus erythematosus, diabetes mellitus, aseptic meningitis, systemic scleroderma, adult-onset idiopathic hypoparathyroidism, or membranous glomerulonephritis (claimed). Other autoimmune diseases which may be teated include e.g. Sjogren's disease, rheumatoid arthritis, necrotizing angitis, granulomatous angitis, autoimmune thyroiditis or myasthenia gravis.

Dwg.0/0
FS CPI
FA AB; DCN
MC CPI: B02-C01; B04-B03A; B05-B01J; B06-D09; B14-A01; B14-C03; B14-C09B; B14-D03; B14-N10; B14-N11; B14-N16; B14-N17; B14-S01; B14-S04
TECH UPTX: 20010328
TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Compound: The anti-ADA agent may inhibit enzymatic activity of ADA, or inhibit the binding of ADA to CD26. The anti-ADA agent may be e.g. **pentostatin**, fludarabine monophosphate, 2-chloro-2'-deoxyadenosine, 2'-deoxyadenosine, 3'-deoxyadenosine or dideoxyadenosine. The anti-ADA agent may be e.g. coadministered with an anti-autoimmune disease drug selected from cyclospoprin A, methotrexate, cyclophosphamide, azathioprine or steroids.

L143 ANSWER 2 OF 6 WPIX (C) 2002 THOMSON DERWENT
AN **2000-564607** [52] WPIX
DNC **C2000-168126**
TI Treating **systemic inflammatory response syndrome** by administration of **adenosine deaminase** inhibitor.
DC B02
IN **LAW, W R**

PA (UNII) UNIV ILLINOIS FOUND
CYC 22
PI US 6103702 A 20000815 (200052)* 15p A61K031-70
WO 2000071127 A1 20001130 (200064) EN A61K031-52
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: AU CA US
AU 2000051515 A 20001212 (200115) A61K031-52
EP 1181019 A1 20020227 (200222) EN A61K031-52
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
ADT US 6103702 A US 1999-317678 19990524; WO 2000071127 A1 WO 2000-US13987 20000522; AU 2000051515 A AU 2000-51515 20000522; EP 1181019 A1 EP 2000-936154 20000522, WO 2000-US13987 20000522
FDT AU 2000051515 A Based on WO 200071127; EP 1181019 A1 Based on WO 200071127
PRAI US 1999-317678 19990524
IC ICM A61K031-52; A61K031-70
ICS A61K031-00; A61K031-7076; A61P017-02; A61P029-00
AB US 6103702 A UPAB: 20001018
NOVELTY - Treating **systemic inflammatory response syndrome** (**SIRS**) comprises administration of an **adenosine deaminase** inhibitor to ameliorate the symptoms.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) affecting the factors involved in **SIRS** comprises administration of an **adenosine deaminase** to affect the levels of factors and

(2) treating tissues affected by burns by increasing local concentration of adenosine in the tissues by contacting them with an effective dose of **adenosine deaminase** inhibitors.

ACTIVITY - **Antiinflammatory**.

MECHANISM OF ACTION - **Adenosine deaminase** inhibitor.

USE - Used to treat **SIRS** by reducing the symptoms of **sepsis** (claimed). The method is also used to treat septic shock, burns and diseases e.g. arthritis, autoimmune diseases, ulcers and irritable bowel **syndrome**, **septicemia**, as well as prophylactic or affirmative treatment of a localized or **SIRS** to infection by one or more of several types of organisms including bacteria, viruses, mycobacteria, yeast, protozoa or parasites. The method is also used to treat disorders in which vascular leakage is involved.

ADVANTAGE - The in vivo inhibition of **adenosine deaminase** results in higher local concentrations of endogenous adenosine than before treatment, to provide beneficial effects (e.g. amplification of **antiinflammatory** cytokines and suppression of **proinflammatory** cytokines). The method increases tissue perfusion, it inhibits neutrophil accumulation, adhesion and activation leading to oxygen free-radical-mediated damage of tissue in the locale where the adenosine production is increased. Two advantages of inhibition of **adenosine deaminase** over inhibition of adenosine kinase to treat **SIRS** are that it reduces oxyradical-mediated tissue damage that occurs via adenosine breakdown via the xanthine oxidase pathway and **adenosine deaminase** will not prevent maintenance of cellular high energy adenine nucleotides that occurs via adenosine kinase. The method is simple, likely to be cost effective because it circumvents the need for multiple therapeutic approaches. It avoids **systemic** affects associated with the use of adenosine analogs (e.g. bradycardia). Cytokine **responses** are merely modulated, rather than abated.

In tests on the ability of **pentostatin** to attenuate **sepsis**, rats were treated with a vehicle control (0.9% saline), **pentostatin** (5 mg/kg/12 hour) or the adenosine receptor antagonist, 8-sulfophenyltheo-phylline (SPT) (400 mu g/kg/8 hour). In the control group **sepsis** resulted in elevated TNF- alpha at 4 and 24

hours, in the **pentostatin** group this **response** was attenuated at these times and SPT amplified the **response** at 24 hours but not at 4 hour.
Dwg.0/13
FS CPI
FA AB; DCN
MC CPI: B06-D09; **B14-A01**; **B14-A02**; **B14-A03**; **B14-A04**; **B14-B02**; **B14-C03**; B14-C09; B14-D07; B14-E08; B14-E10C; **B14-G02D**; B14-N17A; **B14-S06**
TECH UPTX: 20001018
TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred materials: The inhibitor is **pentostatin, EHNA** or **ARADS**. In method (1), the factor is TNF and the factor is affected by reducing levels below those in comparable mammals that are septic and had not been treated with an **adenosine deaminase** inhibitor. The factor can also be thiobarbituric acid reactive substance (TBARS) which is affected by diminution of the level of TBARS or the factor is systemic vascular responses after induction of **sepsis** which is affected by increased blood flow.

L143 ANSWER 3 OF 6 WPIX (C) 2002 THOMSON DERWENT
AN **2000-465868** [40] WPIX
DNC **C2000-140307**
TI Composition comprises a cytotoxic compound and an immunostimulant for the treatment of diseased tissues and organs.
DC B05 D16
IN LEE, C C; LEE, F
PA (LEEC-I) LEE C C; (LEEF-I) LEE F
CYC 22
PI WO 2000040269 A2 20000713 (200040)* EN 24p A61K045-06
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: AU CA CN JP
AU 2000034694 A 20000724 (200052) A61K045-06
ADT WO 2000040269 A2 WO 2000-US191 20000105; AU 2000034694 A AU 2000-34694 20000105
FDT AU 2000034694 A Based on WO 200040269
PRAI US 1999-114906P 19990105
IC ICM A61K045-06
AB WO 200040269 A UPAB: 20000823
NOVELTY - Composition comprises a cytotoxic compound and an immunostimulant which enhances or elicits as immune responses in a host animal in a vehicle for local delivery.
DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for a method for treating tissue affected by microbial or viral infection, or cancerous tissue comprising applying a cytotoxic agent in combination with an immunostimulating agent in a carrier to a site in a patient in need of treatment.
ACTIVITY - Cytostatic; antiviral; antibacterial; antiinflammatory.
MECHANISM OF ACTION - None given.
USE - For the treatment of diseased tissues and organs such as bacterial infected abscesses, virally inflamed tissues, various tumors usually associated with bacterial and viral infection and/or unregulated cellular activities such as inflammation.
Dwg.0/0
FS CPI
FA AB; DCN
MC CPI: B02-Z; B04-C02; B04-E01; B04-F01; B04-F02; B04-F07; B04-F08; B04-F10; B04-H02; B04-H05; B04-H06; B04-J01; B04-L01; B04-M01; B04-N01; B04-N04; B05-A01B; B05-A03B; B06-H; B07-H; B10-B01; B10-B02; B10-B03; B10-B04; B10-C04; B14-A01; B14-A02; B14-A04; B14-C03; B14-D01; B14-D03; B14-G01; B14-H01; B14-L06; D05-A02C; D05-H12; D05-H12E; D05-H16

TECH UPTX: 20000823

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Composition: The cytotoxic compound is selected from alkylating agents, antibiotics, antifungals, antiamebics, antiseptics, antivirals, antimetabolites, inorganic and organic compounds, metal chelators, enzymes, enzyme inhibitors, hormones and hormone analogs, platinum complexes, and other antineoplastic compounds. The immunostimulant is selected from mucopolysaccharides, pyrogens, exotoxins, bacterial cell walls and fragments thereof, DNA/RNA, microorganisms, plant allergens, mammalian cytokines, animal allergens, and synthetic immunostimulants. The alkylating agent is selected from nitrosoureas, nitrogen mustards, methanesulfonates, epoxides, ethylimine, and plant derived alkaloids. The antibiotic is selected from aminoglycosides, amphenicols, ansamycins, beta-lactams, lincosamides, macrolides, tetracyclines, aclacinomycins, actinomycin F1, anthramycin, bleomycins, chromomycins, dactinomycin, daunorubicin, doxorubicin, idarubicin, mitomycins, porfiromycin, streptoigrin, tubercidin, and zinostatin. The antimetabolite is selected from folic acid analogs, purine analogs, pyrimidine analogs, triphosphate (2-fluoro-ara-ATP), 5-fluorouracil, pentosatatin, and hydroxy urea and there derivatives. The inorganic compound is hydrochloric acid, sodium hydroxide, silver nitrate, sulfuric acid, and cesium chloride. The organic compound is acetic acid, formic acid, L-ascorbic acid, ethanol, isopropanol, and dimethylsulfoxide. The metal chelator is EDTA, deferoxamine, sodium ditiocarb, calcium disodium edetate, sodium edetate, trisodium edetate, penicillamine, calcium trisodium pentetate, pentetic acid, succimer, trientine and their derivatives. The enzyme is asparaginase. The antiviral agent is selected from purines/pyrimidinones, acemannan, acetylleucinemonoethanolamine, amantadine, amidomycin, delvirdine, foscarnet sodium, indinavir, interferons, kethoxal, iysozyme, methisazone, moroxydine, nevirapine, podophyllotoxin, ribavirin, rimantadine, ritonavir, saquinavir, stallimycin, statolon, tromantadine, xenazoic acid. The antineoplastic compound is aceglatone, adozelesin, altretamin, aminopterin, amsacrine, anthrcycline, AR102, Arimidex, 5-azacytidine, 5-aza-2-deoxycytidine, betamethasone sodium, bisnafide, bisantrene, 2B1 bispeecific murine Mab, bizelestrin, bropirimine, bryostatin 1, BUDR, campath-1H, capecitabine, chloroquinoxaline sulfonamide, CI-980, cordycepin, crisnatol, cytotoxic cytokines, defosfamide, demecolcine, diaziquone, diethyl homospermine, dihydro-5-azacytidine (DHAC), distamycin (allimustine), (alpha)-difluoromethyl-ornithine (DFMO), docetaxel, 5- or 6-((2,3-bis(hexadecanoyloxy)propyl)phosphanato)ethylcarbamoyl-3,6-O,O-bis(2-nitrobenzyl)-fluorescein sodium salt (DPPE), droloxifene, DTIC-DME, EGF fusion toxin, anti-EGFr chimeric Mab, EGM fusion toxin, eflornithine, elliptinium acetate, estramustine phosphate sodium, amifostine, etoposide, etoglucid, exemestane, fenretinide, filgrastim, filmix, gallium nitrate, gemcitabine, glucosamylmuramyl, tripeptide dipalmitoylglycerol, guanine arabinoside, homoharringtonine, hydroxyurea, idarubicin, isoxifene, irinotecan, idoxuridine (IUDR), LDI-200 letrozole, liarozole, linomide roquinimex, lonidamine, miltefosine, mitotane, matulane, MDX-447, MDX-H210, mitalactol, mitoguazone, mitoxantrone, mopidamol, navelbine, nitracine, octreotide pamoate, oxaliplatin, paclitaxel, peldesine, **pentostatin**, phenamet, phenylacetate, N-phosphonoacetyl-L-aspartic acid, piritraxim, plicamycin, podophyllinic acid 2-ethyl-hydrazide, procarbazine, prazine, radinyl etanidazole, radiolabeled Mab CC-49, razoxane, 9-cis-retinoic acid, RMP-7, SU101, sobuzoxane, spirogermanium, TBC-CEA, temozolomide, teniposide, tenuzonic acid, thalidomide, tirapazamine, topotecan, toremifene, triaziquone, 2,2,2-trichlorotriethylamine, VX-710, timetraxate glucuronate, tretinoin and urethan. The hormone or analog is selected from anastrozole, flutamide, nilutamide, tamoxifen sulfate, diethylstilbestrol and chlorotrianisene. The mucopolysaccharide is chondroitin sulfates A, B, or C, hyaluronic acid or other glucosoaminoglycans. The pyrogen is selected from chemical pyrogens, microbial endotoxins, fragments of microbial endotoxins and lipid A. The bacterial cell wall fragments are pieces and fragments of the

cell walls of microorganisms are from Bordatella pertussis, Corynebacterium parvum, Eubacterials, Mycobacterium avium, Mycobacterium bovis, Mycobacterium fortuitum, Mycobacterium kansaasii, Mycobacterium phlei, Mycobacterium smegmatis, Mycobacterium tubercolosis, Mycobacterium vaccae, Nocardia rubra, Nocardia asteroides and Rhodooccus. They are generated by mechanical shearing, thermal denaturation or chemical disruption of microbial cell walls. The components of the cell wall are lipopolysaccharide, lipoteichoic acid, peptidoglycan, muramyl dipeptide (N-acetylmuramyl-L-alanyl-D-isoglutamine), derivatives of mycolic acids and their complexes. The DNA and RNA are bacterium DNA fragments containing CG motif, RNAs, or their complexes. The plant allergen is derived from Acer negundo, Agrostis alba, Alnus incana, Ambrosia elatior, Artemisia tridentata, Betula alba, Bromus inermus, Cynodon dactylon, Dactylis glomerata, Fraxinus pennsylvanica, Iva xantifolia, Juglans nigra, Juniperus scopulorum, Kochia scoparia, Poa pratensis, Populus nigra italica, Quercus rubra, Secale cerale, Sorghum halepense, Ulmus pumilazea mays, poison hemlock, poison ivy, poison oak. The animal allergen is an ant, bee centipede, cone shell, Gila monster, jellyfishes, keyhole limpet, kissing bug, millipede, mosquitoe, puss caterpillar, scorpions, scorpion fish, sea anemone, sea urchins, snakes, spiders, spotted octopus, starfishes, stonefish, weever fish. The synthetic immunostimulants are Levamisole, Isoprinosine and their derivatives and the exotoxins are microbial exotoxins or fragments thereof, selected from mycotoxins, diphtheria exotoxin, tetanus toxoid, butulinus toxoid. The macrophage stimulating factor is a granulocyte-macrophage colony stimulating factor or a macrophage inflammatory protein, and the mammalian cytokine is an interferon or an interleukin.
Preferred Method: The cytotoxic agent and the immunostimulant are applied sequentially or stimultaneously, locally to the diseased tissue, in a controlled or sustained delivery carrier. .

L143 ANSWER 4 OF 6 WPIX (C) 2002 THOMSON DERWENT
AN **1996-277475** [28] WPIX
DNC **C1996-088018**
TI Compsns. for treatment of fungal infections, parasitic infections or neoplastic disorders - comprise adenosine deriv. e.g. 3'-deoxy adenosine, deaminase inhibitor and carrier.
DC B02 C02 D13
IN MCCAFFREY, R P; SUGAR, A M; WIGZELL, H L R
PA (UYHO-N) UNIV HOSPITAL
CYC 66
PI WO 9616664 A1 19960606 (199628)* EN 52p A61K031-70
RW: AT BE CH DE DK ES FR GB GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG
W: AM AT AU BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE HU IS JP KE KG KP KR KZ LK LR LT LU LV MD MG MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TT UA UG UZ VN
AU 9642411 A 19960619 (199640) A61K031-70
US 5663155 A 19970902 (199741) 12p A61K031-70
EP 794787 A1 19970917 (199742) EN A61K031-70
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE
US 5679648 A 19971021 (199748) 13p A61K031-70
JP 10511345 W 19981104 (199903) 54p A61K031-70
ADT WO 9616664 A1 WO 1995-US15116 19951130; AU 9642411 A AU 1996-42411 19951130; US 5663155 A US 1994-351068 19941130; EP 794787 A1 EP 1995-940768 19951130, WO 1995-US15116 19951130; US 5679648 A US 1994-351067 19941130; JP 10511345 W WO 1995-US15116 19951130, JP 1996-518891 19951130
FDT AU 9642411 A Based on WO 9616664; EP 794787 A1 Based on WO 9616664; JP 10511345 W Based on WO 9616664
PRAI US 1994-351068 19941130; US 1994-351067 19941130
REP 5.Jnl.Ref; JP 52130991
IC ICM A61K031-70

ICS A61K031-17; A61K031-34; A61K031-415; A61K031-44; A61K031-505; A61K031-52; A61K033-24; A61K035-12; A61K035-14; A61K035-16; A61K035-28; A61K045-00; C07H019-16
ICA C07H019-167; C12N009-99
AB WO 9616664 A UPAB: 19960731
A pharmaceutical compsn. comprising an adenosine deriv., a deaminase inhibitor and a carrier is claimed.

Also claimed are (1) treatment or prevention of infection caused by parasites, fungi or fungal-like organisms, comprising admin. of an adenosine deriv.; (2) treatment of neoplastic disorders comprising admin. of an adenosine deriv. and (3) treatment of prevention of infection of biological prods. caused by parasites, fungi or fungal-like organisms, comprising contacting the biological prod. with an adenosine deriv.

The adenosine deriv. is 3'-deoxy-adenosine. The deaminase inhibitor is **deoxycoformycin**. The carrier is selected from water, oils, salts, saccharides, glycerols, polysaccharides and collagens. The adenosine deriv. may be coupled to the deaminase inhibitor.

The compsn. may also contain amphotericin B, sulphadiazine, antibiotics, flucytosine, mycoconazole, fluconazole, itraconazole, ketoconazole, griseofulvin, alkylating agents, purines and pyrimidine analogs, vinca and vinca-like alkaloids, etopsides and etopside-like drugs, antibiotics, corticosteroids, nitrosoureas, antimetabolites, platinum-based cytotoxic drugs, hormonal antagonists, anti-androgens and/or anti-oestrogens.

Admin. of the adenosine deriv. is parenteral, sublingual, enteral, by pulmonary absorption or topical.

USE - The methods may be used to treat or prevent a wide range of fungal, parasitic and other infections, such as filariasis, sarcocystis, trypanosomiasis, leishmaniasis, actinomycosis, tinear pedis candidiasis, aspergillosis, cryptococcosis or coccidioidomycosis in humans and animals.

They may also be used to treat neoplasms such as leukaemias, lymphomas, sarcomas, carcinomas, neural cell tumours, squamous cell carcinomas, germ cell tumours, undifferentiated tumours, seminomas, melanomas, neuroblastomas, mixed cell tumours, metastatic neoplasias and neoplasias due to pathogenic infections.

They may also be used to prevent infection of, e.g., blood, fractionated blood, plasma, serum, bone marrow or transplantable organs, food prods. (such as rice, wheat, barley, breads, oils, spices, dairy prods., fruit and vegetables), or biological prods. derived from living cells (e.g. cytokines, antibodies, recombinant proteins and immune system regulators).

Effective serum levels of the adenosine deriv. or deaminase inhibitor, admin. by any method, are 0.01nM-1.0mM (pref. 0.01nM-1.0mM).
Dwg.0/1
FS CPI
FA AB; DCN
MC CPI: B02-C01; C02-C01; B04-B03A; C04-B03A; B14-A04; C14-A04; B14-B02; C14-B02; B14-D07; C14-D07; B14-H01; C14-H01; D03-H02E
ABEQ US 5663155 A UPAB: 19971013
A method for the treatment of a patient infected with a trypanasonal parasite, comprises administering a therapeutically effective amount of a purine nucleoside and a deaminase inhibitor.
Dwg.0/0
ABEQ US 5679648 A UPAB: 19971209
Treatment of fungal or fungal-like infections comprises administering a purine nucleoside of formula (I).

R1-R3 = H, OH, halo, alkyl, alkoxyl, amine, amide, sulphhydral, nitryl, phosphoryl, sulphinyl or sulphonyl.
Dwg.0/1

L143 ANSWER 5 OF 6 WPIX (C) 2002 THOMSON DERWENT
AN **1996-116345** [12] WPIX
DNC **C1996-036806**

TI New erythro-hydroxy-nonyl-adenine derivs. - useful as adenosine deaminase inhibitors.
DC B02
IN ABUSHANAB, E
PA (CYPR-N) CYPROS PHARM CORP
CYC 1
PI US 5491146 A 19960213 (199612)* 15p A61K031-52
ADT US 5491146 A CIP of US 1993-4721 19930114, US 1994-308590 19940919
PRAI US 1994-308590 19940919; US 1993-4721 19930114
IC ICM A61K031-52
ICS C07D473-18; C07D473-32; C07D473-34
AB US 5491146 A UPAB: 19960322
The following cpds. are new: (1)9-(2(S),9-dihydroxy-3(R)-nonyl)-adenine (I) and its salts; (2) 9-(2(S),8-dihydroxy-3(R)-nonyl)-adenine (II) and its salts; (3) isomers of (I) and (II); (4) analogues of (I) having a substit. other than H or OH on C-9 of the side chain; (5) analogues of (II) having a substit. other than H or OH on C-9 (C-8 may be intended) of the side chain; and (6) erythro-hydroxynonyladenine (**EHNA**) analogues consisting of an erythro-hydroxynonyl side chain attached to an adenyl structure, where the side chain is substd. on a C atom other than C-8 or C-9 by a gp. not normally present in **EHNA**; provided that the cpds. of (2)-(6) inhibit adenosine deaminase (ADA) with a Ki of 10-7 to 10-10.

Also claimed is the synthesis of a hydroxylated **EHNA** analogue in which an erythro-hydroxynonyl side chain attached to an adenyl structure is substd. by at least one gp. not normally present in **EHNA**.

Also claimed is a method for inhibiting ADA in a patient receiving a drug that is degraded by ADA, comprising admin. of an **EHNA** analogue in which an erythro-hydroxynonyl side chain is substd. by at least one gp. not normally present in **EHNA**.

USE - The method is useful for inhibiting ADA-induced degradation of nucleoside analogues used to treat cancer or viral infections. ADA inhibitors can also be used to create ADA deficiencies, which are of interest to researchers.

Dwg.0/4
FS CPI
FA AB; DCN
MC CPI: B06-D09; B14-A02; B14-H01B

L143 ANSWER 6 OF 6 WPIX (C) 2002 THOMSON DERWENT
AN **1994-279378** [34] WPIX
DNC **C1994-127463**
TI Use of adenosine deaminase inhibitors - for prophylaxis and treatment of, e.g., ischaemic conditions.
DC B02 C02
IN ERION, M D; FIRESTEIN, G S; GRUBER, H E; YOUNG, M A
PA (GENS-N) GENSIA INC
CYC 42
PI WO 9417809 A1 19940818 (199434)* EN 32p A61K031-70
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL OA PT SE
W: AT AU BB BG BR CA CH CN CZ DE DK ES FI GB HU JP KP KR LK LU MG MN MW NL NO NZ PL PT RO RU SD SE SK UA UZ
AU 9462972 A 19940829 (199501) A61K031-70
ADT WO 9417809 A1 WO 1994-US1184 19940202; AU 9462972 A AU 1994-62972 19940202, WO 1994-US1184 19940202
FDT AU 9462972 A Based on WO 9417809
PRAI US 1993-14160 19930203
REP 10Jnl.Ref; US 4364922; US 4673563; US 4912092; US 5104859; US 5231086
IC ICM A61K031-70
AB WO 9417809 A UPAB: 19941013
A method for preventing or treating a condition characterised by ischaemia in a mammal comprises administering to the mammal an amt. of a cpd. which

inhibits adenosine deaminase (AD) activity in the mammal but does not cause significant immunodeficiency in the mammal.

The amt. of the cpd. provides less than 95% inhibition of AD activity. The cpds. is pref. administered over less than 3 hrs. The cpd. pref. comprises coformycin, 2'-**deoxycoformycin**, or **erythro-9-(2-hydroxy-3-nonyl)adenine**. The **sepsis** to be treated results from infection with an organism selected from gram negative or positive bacteria, viruses, mycobacteria, fungi yeast or worms, or from endotoxaemia, or from a condition selected from a burn, gunshot wound, perforated bowel, chemotherapy treatment, leucopenia, abdominal surgery or a crological procedure.

USE - The method can be specifically utilised for prophylaxis and treatment of, e.g., myocardial infarction, stroke, angina, **sepsis**, toxic shock, thrombosis, arthritis or atherosclerosis.

Dwg.0/2

FS CPI

FA AB; DCN

MC CPI: B02-C01; C02-C01; B06-D09; C06-D09; B14-A01; C14-A01; B14-C09; C14-C09; B14-D07; C14-D07; B14-F01B; C14-F01B; B14-F01D; C14-F01D; B14-F01E; C14-F01E; B14-F04; C14-F04; B14-F07; C14-F07; B14-N16; C14-N16

=> d his

(FILE 'HOME' ENTERED AT 06:46:45 ON 24 JUN 2002)
SET COST OFF

FILE 'REGISTRY' ENTERED AT 06:46:54 ON 24 JUN 2002
E PENTOSTATIN/CN
L1 1 S E3
E C11H16N4O4/MF
L2 12 S E3 AND OC4/ES AND NCNC2-NCNC4/ES
L3 5 S L2 NOT (LABELED OR (D OR T)/ELS OR 14C OR 3 3 DEOXY)
L4 5 S L1,L3
E C11H15FN4O4/MF
L5 6 S E3
L6 4 S L5 AND OC4/ES
E EHNA/CN
L7 1 S E3
E C14H23N5O/MF
L8 16 S E3 AND NCNC2-NCNC3/ES AND 2/NR
L9 5 S L8 NOT ETHANOL
L10 11 S L8 NOT L9
L11 9 S L10 NOT HEPTYL
L12 7 S L11 NOT (DIMETHYLAMINO OR METHYLAMINO)
L13 7 S L7,L12
E ARADS/CN
L14 STR
L15 2 S L14 CSS SAM
L16 11 S L14 CSS FUL
SAV L16 CRANE994923/A
L17 27 S L4,L6,L13,L16
SEL RN
L18 14 S E1-E27/CRN

FILE 'HCAPLUS' ENTERED AT 07:02:49 ON 24 JUN 2002
L19 833 S L17 OR L18
L20 470 S PENTOSTATIN OR EHNA OR ARADS
L21 694 S DEOXYCOFORMYCIN# OR DEOXY()(COFORMYCIN# OR CO FORMYCIN#) OR C
L22 404 S 2#()(DEOXYCOFORMYCIN# OR DEOXY()(COFORMYCIN# OR CO FORMYCIN#)
L23 370 S ERYTHRO(A)9()2 HYDROXY# 3()(NONYLADENINE OR NONYL ADENINE)

```
L24         1344 S L19-L23
                 E LAW W/AU
L25            9 S E3,E14
                 E LAW WILL/AU
L26           34 S E4,E9,E10
L27            2 S L24 AND L25,L26

     FILE 'REGISTRY' ENTERED AT 07:08:15 ON 24 JUN 2002
L28            3 S ADENOSINE DEAMINASE/CN
L29          102 S ADENOSINE DEAMINASE NOT L28

     FILE 'REGISTRY' ENTERED AT 07:09:38 ON 24 JUN 2002

     FILE 'HCAPLUS' ENTERED AT 07:11:16 ON 24 JUN 2002
L30         3645 S L28
L31           73 S L29
L32          291 S (EC OR "E C")()3 5 4 4
L33         5666 S ADENOSINE DEAMINASE
L34           91 S ADENOSINE AMINOHYDROLASE OR DEOXYADENOSINE DEAMINASE OR ADAR
L35         5954 S L30-L34
L36          812 S L24 AND L35
                 E SEPSIS/CT
                 E E3+ALL
L37         7515 S E4,E3+NT
L38        17209 S E3,E7-E10,E13/BI
L39          607 S SYSTEMIC (L) ?INFLAM? (L) RESPONSE (L) SYNDROM?
L40          375 S SIRS
L41            8 S L24 AND L37-L40
L42            7 S L35 AND L41
                 E SHOCK/CT
                 E E4+ALL
L43        10125 S E5,E6,E4+NT
L44         3392 S E23+NT
L45            4 S L24 AND L43,L44
L46            6 S L24 AND SHOCK
L47            2 S L24 AND CIRCULATORY COLLAPSE
L48           13 S L27,L41,L42,L45-L47
L49            3 S DCF AND L37-L40,L43,L44
L50            3 S DCF AND (SHOCK OR CIRCULATORY COLLAPSE)
L51           18 S L48-L50
                 SEL DN AN 1 7 9 12 14 15
L52            6 S E1-E16 AND L51
L53           12 S L51 NOT L52
                 SEL DN AN 6 8 9
L54            3 S L53 AND E17-E25
L55            9 S L52,L54
L56            1 S CIRCULATORY SHOCK AND L24
L57            9 S L55,L56
L58           35 S L24 AND ?INFLAM?
L59            9 S L24 AND FREE RADICAL
L60           69 S L24 AND ?PERFUSION?
L61            0 S L24 AND MULTI?(L)ORGAN(L)FAIL?
                 E MULTIPLE ORGAN FAILURE/CT
                 E E3+ALL
L62          505 S E3,E2+NT
L63         1085 S E9+NT
L64            0 S L24 AND L62,L63
L65           22 S BLOOD (L) FLOW? AND L24
L66            4 S L57 AND L58-L65
L67            9 S L57,L66
L68           59 S L58,L59,L65 NOT L67
                 SEL DN AN 17 30 45 46
L69            4 S E1-E12 AND L68
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L70          13 S L67,L69
L71          10 S L35 AND L39,L40,L43,L44
L72           2 S L35 AND  CIRCULATORY()(SHOCK OR COLLAPSE)
L73          18 S L71,L72,L70
                SEL DN 9 10 16 17 18
L74          13 S L73 NOT E13-E17
L75          13 S L74 AND (L24 OR DCF OR 2DCF OR L35 OR SEPT? OR SHOCK OR ?CIRC
                E BLOOD VESSEL/CT
                E E3+ALL
L76          48 S L24 AND E5,E4+NT
L77         152 S L24 AND E3+NT
                E E47+ALL
L78          27 S L24 AND E3+NT
L79           7 S L76-L78 AND L75
L80           6 S L75 NOT L79
L81          13 S L75,L79,L80
L82         136 S L24,L35 AND (PERFUSION OR REPERFUSION)
L83           4 S L82 AND L81
L84          13 S L81,L83
                SEL HIT RN

     FILE 'REGISTRY' ENTERED AT 07:48:49 ON 24 JUN 2002
L85           4 S E1-E4
L86          29 S L17,L85

     FILE 'REGISTRY' ENTERED AT 07:49:27 ON 24 JUN 2002

     FILE 'HCAPLUS' ENTERED AT 07:49:58 ON 24 JUN 2002

     FILE 'MEDLINE' ENTERED AT 07:50:38 ON 24 JUN 2002
L87        1753 S L24 OR DCF OR 2DCF
                E SEPSIS/CT
                E E3+ALL
L88       46562 S E4+NT
L89       67559 S E4,E6-E11,E13/BI
L90        5841 S SEPTIC SHOCK
                E SEPSIS/CT
                E E4+ALL
L91        1202 S E11+NT
L92        1886 S E11,E18/BI
L93       69959 S L38,L39,L40
L94        2109 S CIRCULATORY(L)(COLLAPSE OR SHOCK)
L95          15 S L87 AND L88-L94
L96        5769 S L35
L97           5 S L95 AND L96
L98          10 S L95 NOT L97
                SEL DN AN 1-5
L99           5 S L98 NOT E1-E15
L100         10 S L97,L99

     FILE 'MEDLINE' ENTERED AT 07:58:19 ON 24 JUN 2002

     FILE 'EMBASE' ENTERED AT 07:58:30 ON 24 JUN 2002
L101       2416 S L87
                E SEPSIS/CT
                E E3+ALL
L102      22682 S E1+NT
                E SEPT/CT
                E E70+ALL
L103       7795 S E1+NT
                E SEPTIC DISEASE/CT
                E E3+ALL
                E SEPTIC INFLAMMATORY RESPONSE SYNDROME/CT
```

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L104          1 S E3
                E E3=ALL
L105      65256 S L38-L40
L106         20 S L101 AND L102-L105
L107         17 S L106 AND PY<=1999
                SEL DN 10
L108          1 S L107 AND E1

     FILE 'EMBASE' ENTERED AT 08:06:05 ON 24 JUN 2002

     FILE 'WPIX' ENTERED AT 08:06:12 ON 24 JUN 2002
L109         51 S L20
L110         38 S L21
L111          8 S L23
L112         85 S L109-L111
L113          1 S L112 AND LAW W?/AU
                E R10155+ALL/DCN
                E 403766+ALL/DCN
                E R03766+ALL/DCN
L114         66 S E1
L115          1 S DEOXYCHOLEMYCIN# OR DEOXY CHOLEMYCIN#
L116        105 S L112,L114,L115
L117          1 S L116 AND LAW W?/AU
L118        297 S L32-L34
L119          1 S L118 AND LAW W?/AU
L120          1 S L113,L117,L119
L121         46 S R10155/DCN
L122          5 S RA2F10/DCN
L123          1 S 0023-70001/DCN
L124        107 S L116,L121-L123
L125         21 S L118 AND L124
L126       1663 S ((P210 OR P220 OR P232 OR P241 OR P310 OR P330)(S)(P420 OR P4
L127          4 S L126 AND L124
L128          2 S L125 AND L127
L129          2 S L120,L128
L130          2 S L127 NOT L129
L131         29 S (P210 OR P220 OR P232 OR P241 OR P310 OR P330)/M0,M1,M2,M3,M4
                SEL DN AN 13 14 20 21 23
L132          5 S L131 AND E1-E10
L133          6 S L129,L132
L134         13 S L125 NOT L131
L135         31 S L124 AND (B14-A? OR C14-A? OR B12-A? OR C12-A? OR B14-B02 OR
L136          6 S L124 AND (B14-S06 OR C14-S06 OR B12-A01 OR C12-A01 OR B12-A06
L137          6 S L135 AND L136
L138         11 S L133,L137
                SEL DN AN 7-11
L139          6 S L138 NOT E11-E20
L140          6 S L135 NOT L131,L138
L141          1 S L39,L40 AND L124
L142          2 S L38 AND L124
L143          6 S L139,L141,L142

     FILE 'WPIX' ENTERED AT 08:31:52 ON 24 JUN 2002


=> fil biosis
FILE 'BIOSIS' ENTERED AT 08:33:56 ON 24 JUN 2002
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FILE COVERS 1969 TO DATE.
CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT
FROM JANUARY 1969 TO DATE.
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RECORDS LAST ADDED: 19 June 2002 (20020619/ED)

=> d all tot

L149 ANSWER 1 OF 3 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2002:337943 BIOSIS
DN PREV200200337943
TI Inhibiting **adenosine deaminase** modulates the systemic inflammatory response syndrome in endotoxemia and sepsis.
AU Adanin, Simon; Yalovetskiy, Igor V.; Nardulli, Beth A.; Sam, Albert D., II; Jonjev, Zivojin S.; **Law, William R. (1)**
CS (1) Dept. of Physiology and Biophysics, and Surgery, Univ. of Illinois College of Medicine, 835 S. Wolcott St., Chicago, IL, 60612: wrlaw@uic.edu USA
SO American Journal of Physiology, (May, 2002) Vol. 282 , No. 5 Part 2, pp. R1324-R1332. http://www.ajpcon.org. print.
ISSN: 0002-9513.
DT Article
LA English
AB By pharmacological manipulation of endogenous adenosine, using chemically distinct methods, we tested the hypothesis that endogenous adenosine tempers proinflammatory cytokine responses and oxyradical-mediated tissue damage during endotoxemia and sepsis. Rats were pretreated with varying doses of **pentostatin** (PNT; **adenosine deaminase** inhibitor) or 8-sulfophenyltheophylline (8-SPT; adenosine receptor antagonist) and then received either E. coli endotoxin (lipopolysaccharide; 0.01 or 2.0 mg/kg) or a slurry of cecal matter in 5% dextrose in water (200 mg/kg). Resultant levels of tumor necrosis factor (TNF)-alpha, interleukin (IL)-1beta, and IL-10 were measured in serum and in liver and spleen. Untreated, 2 mg/kg lipopolysaccharide elevated serum TNF-alpha, IL-1beta, and IL-10. PNT dose dependently attenuated, without ablating, the elevation in serum TNF-alpha and IL-1beta and raised liver and spleen IL-10. PNT also attenuated elevation of TNF-alpha in serum, liver, and spleen at 4 and 24 h after sepsis induction, and 8-SPT resulted in higher proinflammatory cytokines. Modulating endogenous adenosine was also effective in exacerbated (8-SPT) or diminished (PNT) tissue peroxidation. Survival from sepsis was also improved when PNT was used as a posttreatment. These data indicate that endogenous adenosine is an important modulatory component of systemic inflammatory response syndromes. These data also indicate that inhibition of **adenosine deaminase** may be a novel and viable therapeutic approach to managing the systemic inflammatory response syndrome without ablating important physiological functions.
CC Biochemical Studies - Proteins, Peptides and Amino Acids *10064
Enzymes - General and Comparative Studies; Coenzymes *10802
Pathology, General and Miscellaneous - Therapy *12512
Pharmacology - General *22002
Physiology and Biochemistry of Bacteria *31000
Medical and Clinical Microbiology - Bacteriology *36002
BC Enterobacteriaceae 06702
Muridae 86375
IT Major Concepts
Enzymology (Biochemistry and Molecular Biophysics); Infection; Pharmacology
IT Diseases
endotoxemia: bacterial disease; inflammatory response syndrome: disease-miscellaneous; sepsis: bacterial disease
IT Chemicals & Biochemicals
8-sulfophenyltheophylline: pharmaceutical; **adenosine deaminase**; interleukin-1-beta; interleukin-10; **pentostatin**: enzyme inhibitor - drug; tumor necrosis factor-alpha

IT Alternate Indexing
Endotoxemia (MeSH); Sepsis (MeSH)
ORGN Super Taxa
Enterobacteriaceae: Facultatively Anaerobic Gram-Negative Rods, Eubacteria, Bacteria, Microorganisms; Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
E. coli [Escherichia coli] (Enterobacteriaceae): pathogen; rat (Muridae)
ORGN Organism Superterms
Animals; Bacteria; Chordates; Eubacteria; Mammals; Microorganisms; Nonhuman Mammals; Nonhuman Vertebrates; Rodents; Vertebrates
RN **9026-93-1Q (ADENOSINE DEAMINASE)**
152166-55-7Q (ADENOSINE DEAMINASE)
214692-96-3Q (ADENOSINE DEAMINASE)
53910-25-1 (PENTOSTATIN)

L149 ANSWER 2 OF 3 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2001:258473 BIOSIS
DN PREV200100258473
TI Inhibition of **adenosine deaminase** attenuates, but does not ablate, the IL-1beta and TNF-alpha response to LPS in vivo.
AU Yalovetskiy, Igor V.; Adanin, Simon; Jonjev, Zivojin S.; Ferguson, James L.; Bosmann, H. Bruce; **Law, William R.**
SO FASEB Journal, (March 8, 2001) Vol. 15, No. 5, pp. A1125. print.
Meeting Info.: Annual Meeting of the Federation of American Societies for Experimental Biology on Experimental Biology 2001 Orlando, Florida, USA March 31-April 04, 2001
ISSN: 0892-6638.
DT Conference
LA English
SL English
AB Endogenous adenosine has been reported to modulate tumor necrosis factor-alpha (TNF-alpha) production in vitro, but its effects in vivo, or on other cytokines relevant to sepsis, are not known. We tested the hypothesis that in vivo inhibition of **adenosine deaminase** with **pentostatin** (PNT) during LPS challenge would reduce serum concentrations of the early cytokines TNF-alpha and interleukin (IL)-1beta, independent of changes in IL-10. Male Sprague-Dawley rats (325-400g) received sterile water (vehicle control) or PNT (0.1 or 0.5 mg/kg) ip. After 60 min, rats were challenged with LPS (2mg/kg ip) or 0.9% saline. Blood samples were collected 2 h after LPS. Serum TNF-alpha, IL-1beta, and IL-10 concentrations (pg/ml) were determined by ELISA. Data (means +- SEM) were analyzed by ANOVA (n=4-8/group). Two hours after LPS, rats exhibited signs of systemic illness, including piloerection, lethargy, and slowed reaction to stimuli. Serum TNF-alpha and IL-1beta were below detection in non-LPS control animals; IL-10 was 82 +- 31. TNF-alpha (3534 +- 1124), IL-1beta(1059 +- 128), and IL-10 (278 +- 41) were elevated in untreated LPS rats. PNT-treated LPS animals had a significant attenuation of TNF-alpha (1118 +- 508 and 527 +- 149) and IL-1beta (726 +- 146 and 479 +- 151) at 0.1 and 0.5 mg/kg doses of PNT, respectively, but had no effect on IL-10. Preventing endogenous adenosine degradation with PNT diminished the in vivo TNF-alpha and IL-1beta response to LPS, independent of changes in IL-10. This novel treatment approach strongly attenuated an early cytokine response to LPS without ablating this important immune function.
CC Biochemical Studies - Nucleic Acids, Purines and Pyrimidines *10062
General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals *00520
Biochemical Studies - Proteins, Peptides and Amino Acids *10064
Biochemical Studies - Lipids *10066
Biochemical Studies - Carbohydrates *10068
Enzymes - General and Comparative Studies; Coenzymes *10802

Blood, Blood-Forming Organs and Body Fluids - Blood and Lymph Studies *15002
Blood, Blood-Forming Organs and Body Fluids - Blood Cell Studies *15004
Immunology and Immunochemistry - General; Methods *34502
BC Muridae 86375
IT Major Concepts
Immune System (Chemical Coordination and Homeostasis)
IT Parts, Structures, & Systems of Organisms
blood: blood and lymphatics; serum: blood and lymphatics
IT Chemicals & Biochemicals
adenosine; **adenosine deaminase**: inhibition;
interleukin-1-beta: early cytokine, lipopolysaccharide response;
interleukin-10; lipopolysaccharide; **pentostatin**; tumor
necrosis factor-alpha: early cytokine, lipopolysaccharide response
IT Methods & Equipment
ELISA: analytical method, detection/labeling techniques
IT Miscellaneous Descriptors
lethargy; piloerection; Meeting Abstract
ORGN Super Taxa
Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
Sprague-Dawley rat (Muridae): male
ORGN Organism Superterms
Animals; Chordates; Mammals; Nonhuman Mammals; Nonhuman Vertebrates;
Rodents; Vertebrates
RN 58-61-7 (ADENOSINE)
9026-93-1Q (ADENOSINE DEAMINASE)
152166-55-7Q (ADENOSINE DEAMINASE)
53910-25-1 (PENTOSTATIN)

L149 ANSWER 3 OF 3 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1988:307007 BIOSIS
DN BA86:24045
TI ADENOSINE POTENTIATES INSULIN-STIMULATED MYOCARDIAL GLUCOSE UPTAKE IN-VIVO.
AU **LAW W R**; RAYMOND R M
CS DEP. SURG. LOYOLA UNIV., STRITCH SCH. MED., MAYWOOD, ILL. 60153.
SO AM J PHYSIOL, (1988) 254 (5 PART 2), H970-H975.
CODEN: AJPHAP. ISSN: 0002-9513.
FS BA; OLD
LA English
AB Myocardial adenosine (ADO) has long been regarded as a regulator of coronary blood flow. In other tissues, such as adipose and skeletal muscle, much attention has focused on the role of ADO as a metabolic regulator of the actions of insulin. In the present study, we determined the effect of ADO infusion on insulin-stimulated myocardial glucose uptake (MGU). Mongrel dogs of either sex were instrumented to obtain arterial-coronary sinus differences for glucose, lactate, and oxygen. These were multiplied by circumflex artery blood flow (Q) to obtain uptake values. Measurements were made before and during hyperinsulinemic (4 U/min)-euglycemic clamp (clamp) with intracoronary infusions of saline, ADO, **adenosine deaminase** (ADA), or nitroprusside (NP).
During clamp, MGU increased from a basal value of 3.0 .+-. 0.8 mg/min (mean .+-. SE) to 5.53 .+-. 0.8 mg/min. Adenosine infusion potentiated this response, raising MGU further to 9.02 .+-. 1.1 mg/min while not significantly affecting lactate or oxygen uptakes. Infusion of ADA confirmed the specificity of the response by blocking the metabolic effect of exogenously infused ADO. When Np was infused, Q increased significantly without altering MGU, indicating that the metabolic response to ADO was independent of the changes it caused in Q. A dose-response relationship existed between ADO and insulin-stimulated MGU. The metabolic response to ADO was more sensitive than the vasodilator response. It is concluded that ADO acts as a regulator of insulin in heart. This metabolic regulation

occurs independent of changes in coronary blood flow.
CC Biochemical Methods - Nucleic Acids, Purines and Pyrimidines *10052
Biochemical Studies - Nucleic Acids, Purines and Pyrimidines 10062
Biochemical Studies - Proteins, Peptides and Amino Acids 10064
Biochemical Studies - Carbohydrates 10068
Metabolism - Carbohydrates *13004
Cardiovascular System - Physiology and Biochemistry *14504
Blood, Blood-Forming Organs and Body Fluids - Blood and Lymph Studies *15002
Endocrine System - Pancreas *17008
BC Canidae 85765
IT Miscellaneous Descriptors
DOG HEMODYNAMICS METABOLIC REGULATION
RN 50-99-7 (GLUCOSE)

64267 Access DB# _____

Search Request Form

Scientific and Technical Information Center

Requester's Full Name: L. Eric Crane Examiner #: 65753 Date: **06/20/02**
Art Unit: 1623 Phone Number: **308-4639** Serial No. **09/994,923.**
Mail Box & Bldg/Room Loc: 8D-14/CM-1 Results Format Preferred: **PAPER [8B-19/CM-1]**

If more than one search is submitted, please prioritize searches in order of need.

****

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, key words, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc., if known. Please attach a copy of the cover sheet, pertinent claims, and/or abstract..

Title of Invention: See attached copy of claims.
Inventors (please provide full names): See attached copy of claims.
Earliest Priority Filing Date: **May 24, 1999**

For Sequence Searches only ***Please include all of the pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.***

Please search for treatment of systemic inflammatory response syndrome (SIRS) by administration of an adenosine deaminase (ADA) inhibitor. (SIRS ≡ Sepsis)
Please also search for the administration of one of the ADA inhibitors the structures of which are provided in the attached figures 1, 10, 11 and 12, and whether SIRS has also been treated therewith. Should get two hits (one US patent and one related PCT).

****

STAFF USE ONLY	**Type of Search**	**Vendors/cost as applicable**
Searcher: Jan	NA Sequence(#) _____	STN ✓
Searcher Phone #: 4498	AA Sequence(#) _____	Dialog _____
Searcher Location: _____	Structure (#) ✓	Questel/Orbit _____
Date Searcher Picked Up: _____	Bibliographic ✓	Dr. Link _____
Date Completed: _____	Litigation _____	Lexis/Nexis _____
Searcher Prep & Review Time: _____	Full Text _____	Seq.Syst'ms _____
Clerical Prep Time: 15	Patent Family _____	WWW/Internet _____
Online Time: +10	Other _____	Other(Specify) _____

PTO-1590 (8-2001)

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jan.delaval@uspto.gov